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# Age and Associated Fibrocystic Changes are Prognostically Significant in Patients with Small Node-Negative (T1a,bN0) Invasive Breast Cancer

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■ **Abstract:** Some patients with small (≤1.0 cm) node-negative (T1a,bN0) invasive breast cancer (IBC) who undergo only local therapy experience recurrences. There is limited information on prognostic factors in these patients. We sought to identify prognostic factors associated with disease-free survival (DFS) and overall survival (OS) in patients with T1a,bN0 IBC. Histologic sections from 273 T1a,bN0 IBC patients treated at M. D. Anderson Cancer Center (MDACC) between 1980 and 1999 were reviewed. Microscopic tumor size; multifocality; histologic type, grade of tumor; presence, type, grade of associated ductal carcinoma in situ (DCIS); presence of fibrocystic changes (FCC) with/without atypia; and lymphovascular invasion were identified. The Kaplan–Meier method was used to evaluate DFS and OS. Median patient age was 58 years, median follow-up period was 10.8 years, and median tumor size was 0.8 cm. Multifocal disease was identified in 26% of cases. At 10 years, the DFS and OS rates were 91% and 88%, respectively. Twenty-one percent of patients had extensive (>50%), and 30% had grade 3 DCIS. Nonproliferative FCC and proliferative FCC with/without atypia were present in 80%, 36%, and 38% of patients, respectively. In univariate analysis, age at diagnosis ($p < 0.0001$), grade ($p = 0.015$), and percent ($p = 0.046$) of DCIS were significantly associated with DFS; presence of FCC was associated with longer DFS and OS. In multivariable models, age and presence of FCC remained significantly associated with survival. Age at diagnosis and associated FCC are significant factors in predicting recurrence in patients with T1a,bN0 IBC. Adjuvant systemic therapy should be discussed with and considered for young patients with T1a,bN0 IBC. ■

**Key Words:** age, fibrocystic changes, node-negative breast cancer, prognostic factors, small breast cancer

As a result of the increased use of breast screening programs over the past two decades, the number of invasive breast cancers (IBC) diagnosed at an early stage has increased significantly. According to the 2005 St. Gallen guidelines (1), endocrine responsiveness of tumors is the major criterion in determining the appropriate treatment modality for early stage breast cancer. However, in clinical practice, nodal status still remains the most important parameter for stratifying patients, and nodal status is the most important parameter by which adjuvant treatment decisions are made.

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Numerous studies of prognostic factors have been conducted in patients with node-negative (T1a,bN0) IBC (2–7), and microscopic tumor size and histologic tumor grade have been reported to be the most relevant factors (4). However, no prognostic factors have been clearly identified for small (≤1.0 cm) T1a,bN0 IBC (8). Fisher et al. (9) reviewed data on 1,259 patients with T1a,bN0 breast cancer from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials, and they reported an overall mortality rate of 8% at 8 years of follow-up, regardless of tumor estrogen receptor status or treatment regimen. It has also been well documented in the literature that the proportion of recurrences increases during the second decade of follow-up in patients with these tumors (9–11). Therefore, determining the prognostic factors in T1a,bN0 IBC would allow the identification of patients at risk for

recurrence who might benefit from adjuvant systemic therapy.

In this retrospective study, we evaluated histopathologic and clinical data for 273 patients with T1a,bN0 IBC who were treated at the University of Texas M. D. Anderson Cancer Center (MDACC) between 1980 and 1999 to identify prognostic factors of disease-free survival (DFS) and overall survival (OS).

## MATERIALS AND METHODS

### Patients

This retrospective study was approved by IRB committee of the MDACC, and informed consents were obtained from all the patients included in the study. Through a search of the Breast Cancer Research Database, we identified 325 IBC patients with primary operable breast tumors of ≤1.0 cm (T1a, >0.1 and ≤0.5 cm; T1b, >0.5 and ≤1.0 cm at the largest dimension) and no axillary lymph node metastases (N0), who had been treated at the MDACC between May 1980 and December 1999. Patients' clinical and follow-up information, including survival data were obtained from medical charts, registry records, and death certificates. Breast conserving surgery was the preferred surgical procedure for most patients (66%). The rest of the patients had either unilateral (33%) or bilateral (1%) mastectomy. Adjuvant radiotherapy, chemotherapy, and hormonal therapy were given to 61%, 3%, and 23% of patients, respectively. The original paraffin-embedded histologic slides from all patients were reviewed by one pathologist (M.G.D.). The size of each invasive tumor was determined by directly measuring the largest diameter of a cross-section of the tumor on histologic sections. Fifty cases that had originally been reported to be ≤1.0 cm were found to be >1.0 cm on the glass slides and were thus excluded from the study. In addition, two patients were excluded because of lymph node metastasis. The final study population included 273 T1a,bN0 patients.

### Histopathologic Features

The following histopathologic features of the tumors were evaluated: microscopic tumor size, histologic type, histologic and nuclear grade of the tumor, infiltrative pattern, stromal reaction, the presence of lymphocytic infiltration, peritumoral lymphovascular invasion, and perineural invasion. We also noted tumor multifocality; the presence, type, and grade of associated ductal carcinoma in situ (DCIS); the presence of lobular carcinoma in situ (LCIS); associated nonproliferative fibrocystic changes (FCC) and proliferative FCC, with and without atypia; and associated fibroadenoma. Nonproliferative FCC included cysts, papillary apocrine change, mild epithelial hyperplasia, and nonsclerosing adenosis. Proliferative FCC without atypia included moderate or florid ductal hyperplasia of usual type, sclerosing adenosis, radial scar, and intraductal papilloma or papillomatosis, whereas proliferative lesions with atypia included atypical ductal and lobular hyperplasia. Tumors were histologically classified according to the World Health Organization classification system (12). Histologic and nuclear grading of the tumors were determined according to Elston-modified Bloom–Richardson criteria (13), and the modified Black and Speer nuclear grading system (14), respectively. Multifocality was defined as the presence of two or more foci of the same tumor, with normal breast parenchyma in between, in the same quadrant of the breast (15).

### Data Analysis

Patient characteristics were tabulated and compared among FCC groups (nonproliferative, proliferative without atypia, and proliferative with atypia) using the chi-square test or Wilcoxon rank sum test, as appropriate. DFS and OS were estimated using the Kaplan–Meier product limit method. DFS was defined as the time from the date of definitive breast surgery to the date of disease recurrence or last follow-up. Data from patients who died without having disease recurrence were censored at the date of death in the DFS analysis. OS was calculated as the time from the date of surgery to the date of death from any cause. Median follow-up was calculated for patients who were alive at the last follow-up visit. The log-rank test was used to compare groups in the univariate analysis. Age and tumor size were considered as both continuous variables in univariate Cox proportional hazards models and as dichotomous variables. A clinically relevant age cutoff point of 40 years was chosen, and both 5 and 10 mm were analyzed as cutoff points for tumor size.

Prognostically significant variables in the univariate analysis and additional variables identified as being of scientific interest were included in multivariate models. Multivariate analysis was performed using the Cox proportional hazards model. Results were considered to be significant at $p < 0.05$.

Statistical analysis was performed using S-plus software version 7.0 (Insightful Corporation, Seattle, WA).

## RESULTS

Two hundred and seventy-three patients with a diagnosis of T1a,bN0 IBC were evaluated in this study. Patient and tumor characteristics are summarized in Table 1. The median age at diagnosis was 58 years (range: 29–86 years), and the median tumor size was 0.8 cm (range: 0.1–1.0 cm). Seventy patients (26%) had T1a tumors, and 203 (74%) had T1b tumors. The median follow-up period among patients still alive at last follow-up was 10.8 years (range: 1.8–26.3 years). Local-regional and distant metastases were observed in 74% and 22% of patients, respectively. Most patients (81%) had invasive ductal carcinoma. Nuclear (56%) and histologic (57%) grades of most tumors were intermediate (grade 2). An infiltrative growth pattern was prominent in 91% of tumors. Cellular, and fibrotic or hyalinized stromal reactions were present in 50% and 47% of patients, respectively. Most tumors (71%) had mild to absent lymphocytic infiltration.

Twenty-one percent of patients had extensive DCIS (>50%), and 30% had grade 3 DCIS. DCIS necrosis was detected in 38% of patients. Associated LCIS and fibroadenoma were identified in 10% and 11% of patients, respectively. Perineural invasion was present in 3% of patients.

### Univariate Analyses of DFS and OS

The median duration of follow-up for patients who were alive at last follow-up was 10.8 years (range: 1.8–26.3 years). At 10 years, the DFS and OS rates for all patients were 91% and 88%, respectively.

In the univariate analysis (Table 2), patients with lower-grade DCIS had a longer duration of DFS than those with higher-grade DCIS ($p = 0.015$). DCIS grade was also inversely proportional to age. Median ages of patients with grades 1, 2, and 3 DCIS were 63 (range: 32–77 years), 61.5 (range: 36–77 years), and 54 years (range: 29–78 years), respectively. Although statistically insignificant, patients who had a single tumor focus had longer duration of DFS than those with multifocal disease ($p = 0.06$). In addition, patients with nonproliferative FCC and proliferative FCC without atypia had a longer duration of OS (Figs. 1 and 2) than those without these changes ($p = 0.001$ and 0.04, respectively). Age at diagnosis was significantly associated with the duration of DFS ($p < 0.0001$; Fig. 3). Patients ≤40 years old had

**Table 1. Summary of Patient and Tumor Characteristics**

| Characteristics | No. of patients (%) |
|---|---|
| **Age (years)** | |
| ≤40 | 20 (7) |
| >40 | 253 (93) |
| **Tumor size** | |
| >1 mm, ≤5 mm (T1a) | 70 (26) |
| >5 mm, ≤10 mm (T1b) | 203 (74) |
| **Histologic type** | |
| Invasive ductal carcinoma | 220 (81) |
| "Favorable types"[1] | 24 (9) |
| Other[2] | 29 (10) |
| **Nuclear grade** | |
| 1 (low) | 36 (13) |
| 2 (intermediate) | 153 (56) |
| 3 (high) | 84 (31) |
| **Histologic grade** | |
| 1 (low) | 67 (25) |
| 2 (intermediate) | 157 (57) |
| 3 (high) | 49 (18) |
| **DCIS[3] percentage** | |
| None | 39 (14) |
| ≤50% | 176 (64) |
| >50% | 57 (21) |
| **DCIS[3] grade** | |
| 1 (low) | 22 (8) |
| 2 (intermediate) | 128 (47) |
| 3 (high) | 83 (30) |
| **Fibrocystic changes** | |
| Nonproliferative | 217 (80) |
| Proliferative without atypia | 103 (38) |
| Proliferative with atypia | 97 (36) |
| **Lymphovascular invasion** | |
| Yes | 29 (11) |
| No | 244 (89) |
| **Multifocality** | |
| Yes | 72 (26) |
| No | 201 (74) |
| **Treatment[4]** | |
| Surgery of primary tumor | 273 (100) |
| Breast conserving surgery | 180 (66) |
| Unilateral mastectomy | 90 (33) |
| Bilateral mastectomy | 3 (1) |
| Lymph node surgery | 231 (85) |
| Radiotherapy | 167 (61) |
| Chemotherapy | 9 (3) |
| Hormonal therapy | 63 (23) |
| **Site of recurrence** | |
| Local-regional | 20 (74) |
| Distant | 6 (22) |
| Unknown | 1 (4) |
| **Margins of patients with local-regional recurrence** | |
| Clear | 16 (60) |
| Positive | 2 (7) |
| Unknown | 2 (7) |

[1]Includes tubular, mucinous, cribriform, and papillary carcinomas.
[2]Includes invasive lobular carcinoma, mixed types, and invasive signet ring cell carcinoma.
[3]DCIS characteristics could not be evaluated for one patient because of missing slides.
[4]Surgery of primary tumor (breast conserving surgery or mastectomy) was followed by sentinel lymph node biopsy or axillary dissection and adjuvant therapies in the number of patients indicated.
DCIS, ductal carcinoma in situ.

**Table 2. Univariate Analysis of Disease-Free Survival (DFS) and Overall Survival (OS) in Patients with Node-Negative Breast Cancer**

| | | 10-year DFS | | | | 10-year OS | | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. | No. of events | Estimate (%) | 95% CI | p | No. of events | Estimate (%) | 95% CI | p |
| All | 273 | 27 | 91 | 88–95 | | 45 | 88 | 84–92 | |
| Age (years) | | | | | | | | | |
| ≤40 | 20 | 8 | 64 | 45–89 | <0.0001 | 4 | 84 | 69–100 | 0.89 |
| >40 | 253 | 19 | 93 | 90–97 | | 41 | 88 | 84–92 | |
| Tumor size | | | | | | | | | |
| ≤5 mm | 70 | 6 | 94 | 87–100 | 0.78 | 9 | 90 | 82–98 | 0.68 |
| >5 mm | 203 | 21 | 90 | 86–95 | | 36 | 87 | 82–92 | |
| Nuclear grade | | | | | | | | | |
| 1 | 36 | 2 | 100 | 100–100 | 0.14 | 5 | 91 | 82–100 | 0.75 |
| 2 | 153 | 13 | 92 | 87–97 | | 27 | 86 | 80–92 | |
| 3 | 84 | 12 | 86 | 79–94 | | 13 | 89 | 82–97 | |
| Histologic grade | | | | | | | | | |
| 1 | 67 | 4 | 96 | 91–100 | 0.46 | 7 | 93 | 87–100 | 0.34 |
| 2 | 157 | 18 | 89 | 84–94 | | 29 | 85 | 79–91 | |
| 3 | 49 | 5 | 92 | 84–100 | | 9 | 89 | 80–99 | |
| DCIS grade | | | | | | | | | |
| None or 1 | 61 | 1 | 100 | 100–100 | 0.02 | 9 | 93 | 86–100 | 0.42 |
| 2 | 128 | 14 | 90 | 85–96 | | 20 | 87 | 81–93 | |
| 3 | 83 | 12 | 86 | 79–94 | | 15 | 86 | 79–95 | |
| DCIS percentage | | | | | | | | | |
| None | 39 | 0 | 100 | 100–100 | 0.046 | 6 | 94 | 87–100 | 0.65 |
| ≤50% | 176 | 19 | 90 | 86–95 | | 31 | 86 | 81–92 | |
| >50% | 57 | 8 | 88 | 79–97 | | 7 | 89 | 81–99 | |
| Nonprolif FCC | | | | | | | | | |
| Yes | 217 | 18 | 92 | 89–96 | 0.049 | 28 | 91 | 87–95 | 0.001 |
| No | 56 | 9 | 87 | 78–96 | | 17 | 76 | 65–89 | |
| Prolif FCC without atypia | | | | | | | | | |
| Yes | 103 | 9 | 92 | 87–98 | 0.67 | 10 | 93 | 88–99 | 0.04 |
| No | 170 | 18 | 91 | 86–96 | | 35 | 84 | 79–90 | |
| Prolif FCC with atypia | | | | | | | | | |
| Yes | 97 | 7 | 95 | 90–99 | 0.28 | 15 | 89 | 83–96 | 0.82 |
| No | 176 | 20 | 89 | 85–94 | | 30 | 87 | 82–93 | |
| LVI | | | | | | | | | |
| Yes | 29 | 3 | 90 | 79–100 | 0.95 | 8 | 89 | 78–100 | 0.25 |
| No | 244 | 24 | 91 | 88–95 | | 37 | 88 | 83–92 | |
| Multifocality | | | | | | | | | |
| Yes | 72 | 11 | 86 | 78–94 | 0.06 | 9 | 90 | 82–98 | 0.41 |
| No | 201 | 16 | 93 | 89–97 | | 36 | 87 | 82–92 | |

CI, confidence interval; DCIS, ductal carcinoma in situ; nonprolif FCC, nonproliferative fibrocystic changes; prolif FCC, proliferative fibrocystic changes; LVI, lymphovascular invasion.

shorter duration of DFS than older patients. Lymphovascular invasion and nuclear and histologic grades were not significantly associated with duration of DFS ($p = 0.95$, 0.14, and 0.46, respectively) and OS ($p = 0.25$, 0.75, and 0.34, respectively).

Tumor size was not statistically significantly associated with DFS and OS, either as a continuous variable or as a dichotomous variable at any of the investigated cutoff points. Only results for tumor size dichotomized at 5 mm are presented.

Patients with nonproliferative FCC had a higher rate of LCIS ($p = 0.02$) and fibroadenoma ($p = 0.01$) than those without nonproliferative changes (Table 3). Patients with proliferative FCC without atypia had higher rates of DCIS ($p < 0.0001$), DCIS necrosis ($p = 0.005$) and fibroadenoma ($p < 0.0001$), and had smaller tumors ($p = 0.002$) than those who did not have proliferative changes without atypia. Patients with proliferative FCC with atypia had a higher rate of LCIS ($p < 0.0001$) than those who did not have proliferative changes with atypia.

### Multivariate Analysis

The multivariate models included variables found to be statistically significant in the univariate analyses and variables considered to be of scientific interest, including all three types of FCC, DCIS, lymphovascular invasion, multifocality, tumor grade, tumor size, and patient age. In addition, LCIS, DCIS necrosis, and fibroadenoma were considered for inclusion in

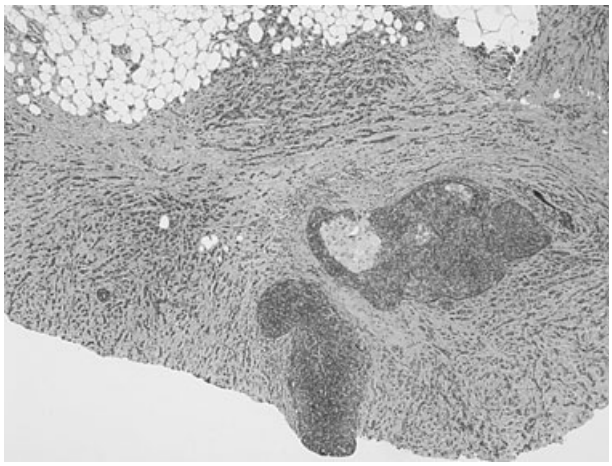


**Figure 1.** Small invasive cancer surrounding ducts that show florid type duct epithelial hyperplasia (H&E, ×20).

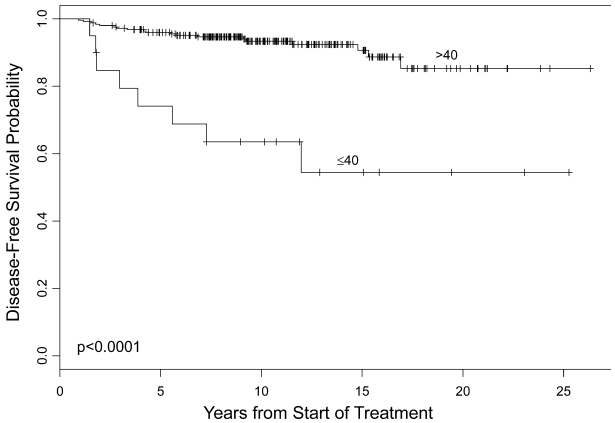



**Figure 3.** Kaplan–Meier estimates of the disease-free survival of patients with node-negative breast cancer by age.

each model because they were found to differ significantly between patients with FCC. However, none of these variables were statistically significant in the multivariate model, and they were thus not included in the final model. As patients with no associated DCIS did not experience recurrences, this variable was collapsed in the DFS model. After we had adjusted for other variables, younger age (p = 0.001) remained significantly associated with DFS, and younger age (p < 0.0001) and nonproliferative FCC (p = 0.006) remained significantly associated with OS (Table 4). Modeling was repeated only for patients with DCIS, so that DCIS grade could be assessed in the multivariate setting. Among patients with DCIS, after we had adjusted for other variables, younger age remained significantly associated with DFS (p = 0.001) and OS (p < 0.0001).

## DISCUSSION

Our findings indicate that young patient age at diagnosis and associated FCC are significant predictors of recurrence in patients with T1a,bN0 IBC. There are only a few studies of T1a,bN0 breast cancer that have included >200 patients, and limited information is available on disease prognosis (3,9,16–18). Thus, uncertainty exists regarding the optimal treatment of these patients (19). Two studies of patients with T1a,bN0 IBC who did not receive adjuvant systemic therapy

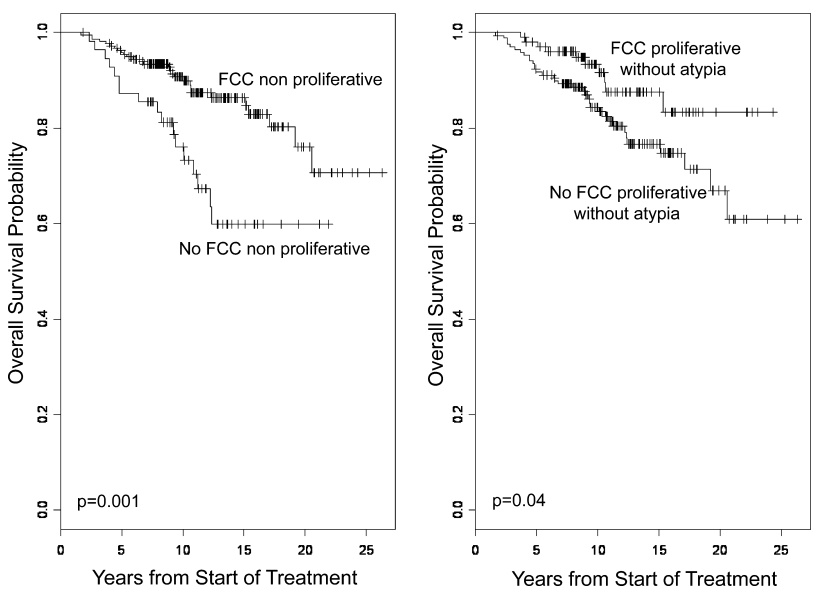



**Figure 2.** Kaplan–Meier estimates of the overall survival of node-negative breast cancer patients by nonproliferative fibrocystic changes and proliferative fibrocystic changes without atypia.

**Table 3. Pathologic Characteristics by Fibrocystic Change Groups**

| | Nonproliferative | | Proliferative without atypia | | Proliferative with atypia | |
|---|---|---|---|---|---|---|
| | No. of patients (%) | p | No. of patients (%) | p | No. of patients (%) | p |
| DCIS percentage | | | | | | |
| None | 29 (13) | 0.11 | 14 (14) | <0.0001 | 16 (16) | 0.75 |
| ≤50% | 137 (63) | | 51 (50) | | 61 (63) | |
| >50% | 51 (24) | | 38 (37) | | 20 (21) | |
| DCIS grade | | | | | | |
| 1 | 19 (9) | 0.66 | 10 (10) | 0.72 | 11 (11) | 0.31 |
| 2 | 104 (48) | | 45 (44) | | 45 (46) | |
| 3 | 65 (30) | | 34 (33) | | 25 (26) | |
| DCIS necrosis | 87 (40) | 0.13 | 50 (49) | 0.005 | 31 (32) | 0.13 |
| LCIS | 26 (12) | 0.02 | 14 (14) | 0.11 | 20 (21) | <0.0001 |
| Fibroadenoma | 30 (14) | 0.01 | 27 (26) | <0.0001 | 16 (17) | 0.05 |

DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

**Table 4. Multivariate Analysis of Disease-Free Survival (DFS) and Overall Survival (OS) for Patients with Node-Negative Breast Cancer**

| | DFS | | OS | |
|---|---|---|---|---|
| Variable | Hazard ratio | p | Hazard ratio | p |
| Age (continuous) | 0.94 | 0.001 | 1.06 | <0.0001 |
| Tumor size (≤5 versus >5 mm) | 2.04 | 0.17 | 0.77 | 0.58 |
| Multifocality (yes versus no) | 2.02 | 0.11 | 0.65 | 0.32 |
| Nuclear grade | | | | |
| 3 versus 1 | 1.74 | 0.48 | 1.53 | 0.44 |
| 2 versus 1 | 1.05 | 0.96 | 1.36 | 0.54 |
| LVI (yes versus no) | 0.53 | 0.33 | 1.55 | 0.30 |
| Fibrocystic changes | | | | |
| Nonprolif (yes versus no) | 0.61 | 0.28 | 0.38 | 0.006 |
| Prolif w/o atypia (yes versus no) | 0.80 | 0.64 | 0.60 | 0.23 |
| Prolif with atypia (yes versus no) | 0.69 | 0.42 | 1.58 | 0.19 |
| DCIS percentage | | | | |
| >50% versus none | 1.79* | 0.29* | 2.23 | 0.21 |
| ≤50% versus none | | | 1.96 | 0.15 |

*>50% versus ≤50% (for computational reasons, ≤50% and none had to be combined for DFS).
LVI, lymphovascular invasion; nonprolif, nonproliferative; prolif, proliferative; w/o, without; DCIS, ductal carcinoma in situ.

reported recurrence-free survival rates of 91% (20) and 82% (2) at 10 years. In two T1a,bN0 IBC studies that summarized data from randomized clinical trials (the Natural History Data Base (21) and the National Surgical Adjuvant Breast and Bowel Project (9)) and in which some patients received adjuvant systemic therapy, 10-year recurrence-free survival and 8-year OS rates of 83% and 92%, respectively, were reported.

Although different study designs, treatment modalities, and outcome variables were used in these studies, it is apparent that there is a subpopulation of patients with T1a,bN0 breast cancer who experience disease recurrence. The tumor characteristics most consistently associated with a poor prognosis are high tumor grade and presence of lymphovascular invasion (16,17,22). Estrogen, progesterone-negative status (18), younger age at diagnosis (3,6,9,18,23), and the presence of proliferation markers such as S-phase fraction have also been suggested as risk factors for recurrence in these patients (24). Hanrahan et al. (18), in a recent study, have reported that age younger than 50 years at diagnosis, high tumor grade, estrogen and progesterone receptor-negative status, and fewer than six nodes removed at axillary dissection were associated with increased risk of breast cancer-specific mortality in patients with T1a,bN0 breast cancer. Our results similarly indicate that patients aged ≤40 years have a poorer prognosis, in terms of both disease recurrence and duration of OS, than do older patients and suggest that T1a,bN0 breast cancer is more aggressive in younger women.

It is well known that margin status is a predictor of local recurrence in breast cancer patients. In our study, most of the patients had negative margin as defined by no DCIS or invasive carcinoma at inked margin. However, because this was a retrospective study, and we had consultation cases with outside excision, it was not possible to measure the clearance of the margin in all cases.

There are also some studies investigating the correlation between mammographic appearance and long-term prognosis in patients with small IBC (25,26). Tabar et al. (25) have reported in their study that except for the small group of patients associated with casting-type calcifications, all the patients with T1a,b breast cancer had excellent survival without extensive

surgery or any adjuvant treatment, independent of lymph node status or histologic grade.

The association between FCC (especially nonproliferative and proliferative without atypia) and longer OS found in our study suggests that associated benign lesions may affect the biologic and clinical behavior of T1a,bN0 breast cancer. Associated benign lesions are not usually thoroughly evaluated in patients with breast cancer, and no specific information exists in the literature regarding the importance of these lesions. We believe that our results will encourage further studies.

The impact of associated FCC on survival rates of patients with small, T1a,bN0 breast cancer may be explained by differences in the molecular or genetic background of IBC. Thus, invasive cancers arising in a background of FCC may have different molecular or genetic aberrations than tumors arising in a background with no associated FCC. It is also important to note that all recurrences in this study were detected in the 77% of patients with associated grade 2 or 3 DCIS. Although there was no significance in terms of DCIS grade in multivariate analysis in our study, we may suggest that patients with T1a,bN0 IBC who have no associated DCIS or who have associated low-grade (grade 1) DCIS can be excluded from receiving adjuvant systemic therapy. Further studies investigating the relation of associated benign or malignant lesions, that is, FCC or DCIS with small, T1a,bN0 IBC are required.

## CONCLUSION

In this retrospective study, age of the patient at diagnosis and associated FCC are significant predictors of recurrence in patients with T1a,bN0 breast cancer. Until more accurate data are obtained for associated benign or malignant lesions with small, T1a,bN0 tumors we suggest that associated lesions (i.e., DCIS and FCC) and multifocality of the tumor should be assessed thoroughly in all cases of IBC. In addition, until more clinically relevant data are gathered, adjuvant systemic therapy should be discussed with and considered for young patients with these small tumors.

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