

Tumor Characteristics and Clinical Outcome of Elderly Women With Breast Cancer

Sami G. Diab, Richard M. Elledge, Gary M. Clark

Background: The number of elderly patients with breast cancer is increasing. Limited age-related information available about this disease prompted this study. **Patients and Methods:** The study population was derived from 50 828 and 256 287 patients with invasive breast cancer in San Antonio breast cancer databases and the Surveillance, Epidemiology, and End Results (SEER) registry, respectively. Tumor biologic and clinical characteristics, local and systemic therapies, and survival according to the patient's age were analyzed. Survival was also compared with that of age-matched women from the general population. **Results:** In patients 55 years old or older, there was an association between increasing age at diagnosis and the presence of more favorable biologic characteristics of the tumor, including more tumors that express steroid receptors, lower proliferative rates, diploidy, normal p53, and absence of the expression of epidermal growth factor receptor and c-erbB2. In older patients with lymph node-negative disease and/or small tumors, the observed and expected survivals were almost identical. In the SEER registry, the 8-year survival of lymph node-negative patients relative to the expected survival of age-matched women from the general population was 1.01 (95% confidence interval [CI] = 0.98–1.04) for patients 70–74 years old, 1.06 (95% CI = 1.01–1.11) for patients 75–79 years old, and 1.09 (95% CI = 0.98–1.20) for patients 80–84 years old. **Conclusion:** In women 55 years old or older, advancing age is associated with more favorable tumor biology, and breast cancer survival in older women is similar to survival in the general population irrespective of disease status. This favorable outcome should be considered when making clinical decisions in older patients. [J Natl Cancer Inst 2000;92:550–6]

The general population of the United States is aging (1). The population 65 years old or older represented 11.3% (25.5 million) of the total population in 1980 and is anticipated to represent 20.1% (70.2 million) by 2030 (2). In addition, there is an upward age shift within the population 65 years old or older. Thirty-two percent of the population 65 years of age or older were 75 years old or older in 1980, compared with an anticipated 51% in 2000 (2). Because the incidence of breast cancer increases with age (3), the changing demographics of the U.S. population will lead to more cases of breast cancer in the population 65 years old or older. Data from the Surveillance, Epidemiology, and End Results (SEER) Program¹ show that 37% of the patients with breast cancer diagnosed in 1973 were 65 years or older compared with 46.7% in 1995 (4). By applying these statistics to the approximately 175 000 new cases of breast cancer in 1998 (3), we estimate that each year more than 80 000 new cases of breast cancer will be diagnosed in women 65 years old or older.

Although the number of elderly patients with breast cancer is

increasing, knowledge about possible differences in the biology and clinical outcomes of breast cancer according to age is limited. The relative underenrollment of patients 65 years old or older in clinical trials is an important factor contributing to this limited knowledge (5). In spite of the paucity of data, physicians consider age to be an important determinant of therapy, and the pattern of care of breast cancer patients differs depending on age (6–10). Clearly, more information about the biology and clinical features of breast cancer is needed to support the different approaches to therapy in elderly patients.

Furthermore, the impact of small breast tumors on the survival of elderly patients is not known. This is an important aspect to explore because the indolent nature of breast cancer in postmenopausal women (11) and the competing causes of mortality from other comorbid conditions might interact with breast cancer and influence its impact on mortality (12–14). The identification of women with indolent tumors who are unlikely to die of their tumors would have a substantial impact on screening strategies and on the clinical management of these patients.

In this study, we have explored the clinical and biologic characteristics of elderly women with breast cancer in the San Antonio breast cancer databases and in the SEER registry. In addition, we have identified specific subsets of elderly patients with breast cancer who have survival that is similar to that expected in the general population irrespective of disease status.

PATIENTS AND METHODS

Study Population

The study population was derived from 50 828 and 256 287 patients with invasive breast cancer who are included in San Antonio breast cancer databases and in the SEER registry, respectively. As reported elsewhere (15,16), patients are included in the San Antonio databases because steroid receptors and other biologic assays were performed in a central laboratory on tissue from primary tumors. More than 370 academic and community institutions have submitted tissue and clinical data. Demographic and survival data were obtained by direct review of the medical records or tumor registry records performed by the data managers of the San Antonio databases or by data collection forms completed by the offices of the referring physicians.

The SEER Program, established in 1973, is a collection of nine population-based cancer registries in the United States, which collect and submit cancer incidence and follow-up data to the National Cancer Institute. The study population was identified from all registered patients with invasive breast cancer from 1973 through 1995 with follow-up information submitted until August 1997 (4). Patients coded as having *in situ* tumors were excluded from this study. The SEER Program started collecting data on tumor size and lymph node status in 1988 and data on steroid receptor status in 1990.

Affiliations of authors: S. G. Diab, Rocky Mountain Cancer Centers—Aurora, CO; R. M. Elledge, G. M. Clark, Breast Center at Baylor College of Medicine, Houston, TX.

Correspondence to: Sami G. Diab, M.D., Rocky Mountain Cancer Centers—Aurora, 1700 S. Potomac St., Aurora, CO 80012 (e-mail: sami.diab@usoncology.com).

See "Notes" following "References."

© Oxford University Press

Prognostic Factors in the San Antonio Databases

Concentrations of estrogen receptor and progesterone receptor were evaluated by the modified dextran-coated charcoal assay (17). For estrogen receptors and progesterone receptors, respectively, levels of 3 fmol/mg or more and 5 fmol/mg or more were considered to be positive. The S-phase fraction (the fraction of tumor cells in S phase of the cell cycle) and DNA ploidy were evaluated by flow cytometry (15,16). S-phase fractions of 6.7% or more for diploid carcinomas and 11.0% or more for aneuploid carcinomas were considered to be high. We determined the c-erbB2 status by western blotting (18). The cutoff value between low and high protein expression was 1 U/μg of protein. Epidermal growth factor receptor was measured by a radiobinding assay, and levels of 10 fmol/mg of protein or more were considered to be positive (19). We determined the p53 status by immunohistochemistry, and negative nuclear staining was a surrogate marker for normal p53 (20).

Survival Data

The beginning and end dates for survival calculations are the date of diagnosis of breast cancer and the date of last follow-up or death, respectively. The observed survival rate is the actual probability of surviving a specific time interval calculated from the cohort of breast cancer patients by the method of Kaplan and Meier (21). The expected survival rate is the probability of surviving the specified time interval in the general U.S. population. For patients in the San Antonio databases, age-matched mortality rates for females from the general population were calculated on the basis of life expectancy tables (1994) from the U.S. National Center for Health Statistics, *Vital Statistics of the United States* (22), which are available through the Library of Congress, Washington, DC.

Expected probabilities in the SEER database have been generated from the U.S. population and are matched to the cohort patients by race, sex, age, and date of diagnosis. Relative survival is the observed survival probability for the specified time interval adjusted for the expected survival. The reported survivals and the 95% confidence intervals (CIs) for patients in SEER are the survival at 8 years except where indicated.

Individual category numbers for the cause of death are those coded according to the ninth revision of the International Classification of Diseases (23). The codes used for breast cancer-related deaths are 1740–1749.

Statistical Methods

The clinical and biologic characteristics of breast cancer according to age were compared by use of contingency tables and Mantel–Haenszel tests for linear associations. Survival curves were estimated by the method of Kaplan and Meier (21). Analyses were performed with SAS® Version 6.11 (SAS Institute, Cary, NC) for patients in the San Antonio databases and with SEER* Stat Version 1.1 provided by the Cancer Statistics Branch of the National Cancer Institute (4). All *P* values are from two-sided tests.

RESULTS

Tumor Characteristics and Therapy Based on Age

Of 50 828 and 256 287 patients with invasive breast cancer in the San Antonio breast cancer and SEER databases, 35 154 (69%) and 171 424 (67%) were 55 years old or older, respectively. Since the SEER Program did not start recording tumor size until 1988 and receptor status until 1990, tumor size is available for 44 598 patients, and progesterone receptor status is available for 43 155 patients. Table 1 summarizes the tumor characteristics according to age of the patient in the San Antonio databases.

There were statistically significant differences in histology based on age, with older patients having more lobular and mucinous carcinomas in both the San Antonio databases (Table 1) and the SEER registry (data not shown). Patients 85 years old or older had larger tumors at diagnosis than younger patients. Only 8% of patients 85 years old or older had tumors smaller than 1 cm compared with 12%–14% of younger patients in the San Antonio databases ($P < .001$). Similarly, in SEER, the percentage of patients 85 years old or older with tumors smaller than 1 cm

Table 1. Tumor characteristics by age group in the San Antonio databases*

Age group	55–64 y	65–74 y	75–84 y	≥85 y
No. of patients	12 101	13 123	7873	2057
Histology				
No. with data	11 882	12 877	7735	2018
NOS,† %	85	83	82	79
Lobular, %	8	9	9	10
Mucinous, %	1	2	4	6
Tubular, %	1	1	1	1
Medullary, %	2	1	1	1
Others, %	3	3	3	4
Tumor size				
No. with data	11 454	12 427	7524	1964
<1 cm, %	13	14	12	8
1–1.9 cm, %	39	41	41	38
2–4.9 cm, %	40	37	38	44
≥5 cm, %	9	8	8	10
Positive lymph nodes				
No. with data	11 545	12 310	6805	1302
0, %	59	65	66	61
1–3, %	22	20	21	24
≥4, %	18	15	14	15
Estrogen receptors				
No. tested	11 970	12 978	7802	2046
Positive, %	83	87	90	91
Progesterone receptors				
No. tested	11 664	12 710	7697	2028
Positive, %	57	63	64	66
Ploidy				
No. tested	10 522	11 716	7311	1947
Diploid, %	46	50	52	52
S-phase fraction				
No. tested	8958	10 124	6313	1704
Low, %	51	57	61	60
Intermediate, %	20	19	19	21
High, %	29	24	20	19
p53‡				
No. tested	478	434	117	23
Negative (normal), %	51	55	59	61
c-erbB2				
No. tested	985	993	536	99
Negative, %	79	85	86	90
Epidermal growth factor receptor§				
No. tested	603	639	367	90
Negative, %	83	85	89	90

*Statistically significant differences ($P < .001$; Mantel–Haenszel test) were found for each variable according to age except where indicated.

†NOS = no special type.

‡ $P = .030$ (Mantel–Haenszel test).

§ $P = .003$ (Mantel–Haenszel test).

was 10% compared with 17%–20% of younger patients ($P = .001$).

In spite of the larger tumor size, older patients had tumors with more favorable biologic characteristics (Table 1). In the San Antonio databases, the older the patients, the higher the likelihood that the tumor had estrogen receptors and progesterone receptors. The number of tumors with estrogen receptors increased from 83% in patients 55–64 years old to 87% in patients 65–74 years old to 90% in patients 75–84 years old to 91% in patients 85 years old or older ($P < .001$). Similar trends were observed for the other biologic characteristics. Compared with younger patients, older patients had more tumors that were diploid, had a low S-phase fraction and normal p53, and were negative for epidermal growth factor receptor and c-erbB2

(Table 1). The data from SEER also supported similar associations between age and favorable biologic characteristics. In SEER, tumors with estrogen receptors were found in 68%, 78%, 83%, and 84% of patients 55–64 years old, 65–74 years old, 75–84 years old, and 85 years old or older, respectively, and a similar trend for tumors with progesterone receptors was noted (data not shown).

The local and systemic therapies for breast cancer differed according to age, with older women receiving less therapy. In the San Antonio databases (Table 2), there was a gradual decrease in the number of patients receiving systemic chemotherapy according to age, with 30%, 16%, 6%, and 1% of patients 55–64 years old, 65–74 years old, 75–84 years old, and 85 years old or older, respectively, receiving such a therapy. On the other hand, adjuvant endocrine therapy was prescribed almost equally in all age groups (36%–38%). Local radiation therapy was also less frequently given to older patients, with 27%, 24%, 18%, and 8% of patients 55–64 years old, 65–74 years old, 75–84 years old, and 85 years old or older, respectively, receiving adjuvant radiation therapy in the San Antonio databases. In addition, older patients in the San Antonio databases were less likely to undergo modified radical mastectomy (64% in patients ≥ 85 years old versus 83% in patients 75–84 years old versus 88% in patients 55–74 years old). Older patients in this database were more likely to undergo partial mastectomy (24% in patients ≥ 85 years old versus 13% in patients 75–84 years old versus 10% in patients 55–74 years old). Similar patterns of local therapy were found in SEER, where fewer older patients received adjuvant radiation therapy. In SEER, 91%, 81%, 73%, and 70% of patients 85 years old or older, 75–84 years old, 65–74 years old, and 55–64 years old, respectively, did not receive radiation therapy and 29% of patients 85 years old or older had a partial mastectomy (SEER site-specific surgery codes 10 and 20) compared with 20%–21% of patients 55–84 years old.

Survival and Age

Because older women have tumors with more favorable biologic characteristics, we hypothesized that specific subsets of

elderly patients with breast cancer might have survival similar to that of the general population. To test this hypothesis, we explored in the SEER database the observed, expected, and relative survivals for different age groups based on lymph node status (Table 3 and Fig. 1) and tumor size (Table 3). As the age of patients with lymph node-negative disease or tumors smaller than 2 cm increased from 50 to 70 years, the observed survival gradually approached the expected survival until ages 70–74 years. In that age group, the observed and expected survivals were almost indistinguishable. Relative survival at 8 years was 1.01 (95% CI = 0.98–1.04) for patients with lymph node-negative disease, 1.01 (95% CI = 0.94–1.08) for patients with tumors smaller than 1 cm, and 1.00 (95% CI = 0.96–1.04) for patients with tumors 1.0–1.9 cm. It is interesting that patients 75 years old or older with lymph node-negative disease and/or small tumors had an observed survival that was superior to the expected survival (Table 3). Although the difference between the observed and expected survivals gradually decreased as age increased in patients with positive lymph nodes, the observed survival was lower than the expected survival. The relative survival at 8 years for patients with one to three positive lymph nodes was 0.74 (95% CI = 0.68–0.8) for patients 50–54 years old, 0.81 (95% CI = 0.76–0.86) for patients 60–64 years old, 0.78 (95% CI = 0.7–0.86) for patients 70–74 years old, and 0.89 (95% CI = 0.71–1.07) for patients 80–84 years old. As expected, the relative survivals for patients with large tumors (>2 cm) or more than three positive lymph nodes were always less than one regardless of age (data not shown).

Similar relationships between age and survival were found in the San Antonio databases. For patients with lymph node-negative disease, the 5-year observed and expected survivals for patients 55–64 years old, 65–74 years old, 75–84 years old, and 85 years old or older were 90% (95% CI = 89%–91%) and 95%, 85% (95% CI = 84%–86%) and 89%, 74% (95% CI = 72%–75%) and 74%, and 53% (95% CI = 49%–56%) and 43%, respectively. On the other hand, the observed survivals for patients with lymph node-positive disease in the San Antonio databases were always lower than the expected survivals (data not shown).

Finally, in the SEER registry, we examined the relative contribution of breast cancer death to the overall causes of mortality based on age of patients with breast cancer (Table 4). Breast cancer was responsible for 73% of all causes of death in breast cancer patients between the ages of 50 and 54 years. This percentage gradually decreased as age increased, with breast cancer being responsible for only 29% of all deaths in patients 85 years old or older. This relative decrease in breast cancer-related mortality was even more pronounced in patients with small tumors, where breast cancer was responsible for only 12%–16% of all deaths in patients 75 years old or older (Table 4).

DISCUSSION

This study clearly demonstrates that breast cancer in the elderly has distinctive biologic and clinical characteristics. Both the San Antonio and the SEER databases show that the percentage of patients with tumors that have steroid hormone receptors increases with age. The San Antonio databases also show that older patients are more likely to have tumors that are diploid with a low S-phase fraction, normal p53, and low or negative

Table 2. Local and adjuvant systemic therapies by age group in the San Antonio databases*

Therapy	Age			
	55–64 y	65–74 y	75–84 y	≥ 85 y
Surgery				
No. of patients	12 057	13 090	7838	2043
Modified radical mastectomy, %	88	88	83	64
Total mastectomy, %	1	1	3	10
Partial mastectomy, %	10	10	13	24
Incisional biopsy, %	1	1	1	3
Adjuvant radiation therapy				
No. of patients	11 124	11 923	6978	1749
Yes, %	27	24	18	8
Adjuvant chemotherapy				
No. of patients	11 125	11 921	6974	1748
Yes, %	30	16	6	1
Adjuvant endocrine therapy†				
No. of patients	11 118	11 917	6974	1747
Yes, %	36	38	38	36

*Statistically significant differences ($P < .001$; Mantel–Haenszel test) were found for each variable according to age except where indicated.

† $P = .02$ (Mantel–Haenszel test).

Table 3. Relative survival*—mean (95% confidence interval)—according to lymph node status and tumor size in the Surveillance, Epidemiology, and End Results (SEER) registry

Age, y	All patients	Lymph node-negative disease	Tumor size	
			<1 cm	1.0–1.9 cm
50–54	0.76 (0.75–0.77)	0.95 (0.93–0.97)	0.96 (0.92–1.00)	0.91 (0.88–0.94)
55–59	0.74 (0.73–0.75)	0.91 (0.88–0.94)	0.98 (0.94–1.12)	0.87 (0.83–0.91)
60–64	0.78 (0.77–0.79)	0.96 (0.94–0.98)	1.02 (0.99–1.05)	0.93 (0.9–0.96)
65–69	0.80 (0.79–0.81)	0.97 (0.95–0.99)	1.03 (0.99–1.07)	0.93 (0.89–0.97)
70–74	0.81 (0.8–0.82)	1.01 (0.98–1.04)	1.01 (0.94–1.08)	1.00 (0.96–1.04)
75–79	0.82 (0.81–0.83)	1.06 (1.01–1.11)	1.05 (0.94–1.16)	1.01 (0.94–1.08)
80–84	0.82 (0.80–0.84)	1.09 (0.98–1.20)	1.21 (0.98–1.43)	1.05 (0.92–1.18)
≥85 (7 y) [†]	0.78 (0.75–0.81)	1.19 (1.04–1.34)	1.18 (0.84–1.52)	1.03 (0.88–1.18)

*Relative survival (95% confidence interval) at 8 years.

[†]Relative survival (95% confidence interval) at 7 years.

levels of epidermal growth factor receptor and c-erbB2. The finding that older patients had larger tumors than younger patients could be explained by a delay in the diagnosis of breast cancer in older patients because of fewer breast (24) and screening mammography (25,26) examinations.

The different approaches to local and systemic treatments in elderly patients with breast cancer have been well documented (6–10). This study demonstrates that elderly patients are less likely to receive systemic chemotherapy and radiation therapy. It also demonstrates that older patients undergo less extensive surgical resection than do younger patients. On the other hand, older patients are just as likely to receive systemic endocrine therapy as younger patients. However, because older patients are more likely to have tumors with steroid hormone receptors, one might expect that a greater proportion should receive adjuvant endocrine therapy. Therefore, it is not clear whether age was a factor in the decision regarding adjuvant endocrine therapy. It is unfortunate that the majority of clinical trials that addressed surgical (27,28), radiation (29,30), and systemic (31) therapies have not included older patients. Therefore, definitive recommendations from these studies might not apply to older patients. The best approaches to local and systemic therapies in elderly patients and the impact of each modality of therapy on the natural history of the disease and the quality of life require evaluation in clinical trials.

One of the most important findings of this study is that the impact of breast cancer on the expected survival of patients decreases with age. For patients with lymph node-negative disease and/or small tumors (<2 cm), the gap between the observed and expected survivals narrowed as the patients aged; in older patients, the observed and expected survivals were almost identical. The finding that the observed and expected survivals in older patients with lymph node-negative disease and/or small tumors are almost identical should not be interpreted as an indication of a lack of substantial mortality from breast cancer. Indeed, breast cancer was the cause of death in 12%–16% of patients 75 years old or older, although these patients had tumors smaller than 1 cm (Table 4). The similarity in the observed and expected survivals of older patients with breast cancer, despite substantial mortality related to breast cancer, suggests that the distribution and impact of other comorbid conditions on survival might be different in the breast cancer population and the population at large. This could be related to the fact that women diagnosed with breast cancer receive more medical attention. The additional medical attention would allow the detection and

treatment of other medical problems, such as hypertension and diabetes, which in turn might reduce the number of deaths related to these conditions. Another attractive explanation is that older patients with breast cancer might have higher levels of or higher sensitivity to endogenous estrogen. They also might be more likely to be on hormone replacement therapy, which might lead to lower cardiovascular risk for developing coronary artery disease and strokes—major causes of mortality in the elderly. It is clear from this study that other competing causes of mortality assume a larger role in determining survival in older patients and that, relative to other causes of death, breast cancer mortality decreases as patients age. Finally, differences in socioeconomic status between patients with breast cancer and the general population might also be contributing factors.

The relationship between survival and age observed in this study was not found in another study of 57 068 Swedish women with breast cancer (32). One reason for this difference is that the Swedish study included patients with all stages of breast cancer and did not separately evaluate patients with small tumors and/or negative lymph nodes, as we did. Indeed, our results are similar to the results of the Swedish study when all patients, regardless of tumor size and lymph node status, are analyzed (Table 3). In addition, the distribution of comorbid conditions might be different in the two populations studied.

The observation that the observed survival is not inferior to the expected survival in older patients with breast cancer has several clinical implications. One implication is related to the use of screening mammography in older patients. The value of screening mammography in decreasing mortality related to breast cancer is established beyond doubt in patients younger than 75 years old (33). However, all of the studies of screening mammography have limited their accrual to patients younger than 75 years old (33). Therefore, the value of screening mammography in patients 75 years old or older has not been studied adequately. The impact of screening mammography on the mortality, morbidity, and quality of life in this age group is not clear (34–36). Because older patients with small tumors are more likely to die of non-breast-cancer conditions and because screening mammography detects small tumors that are more likely to be lymph node negative, it is possible that screening mammography might have limited value in older patients. This is especially true in patients with other comorbid conditions that would be the major causes of mortality in these patients with indolent tumors. Clearly, to determine with certainty the value of screening mammography in elderly patients, randomized clinical trials

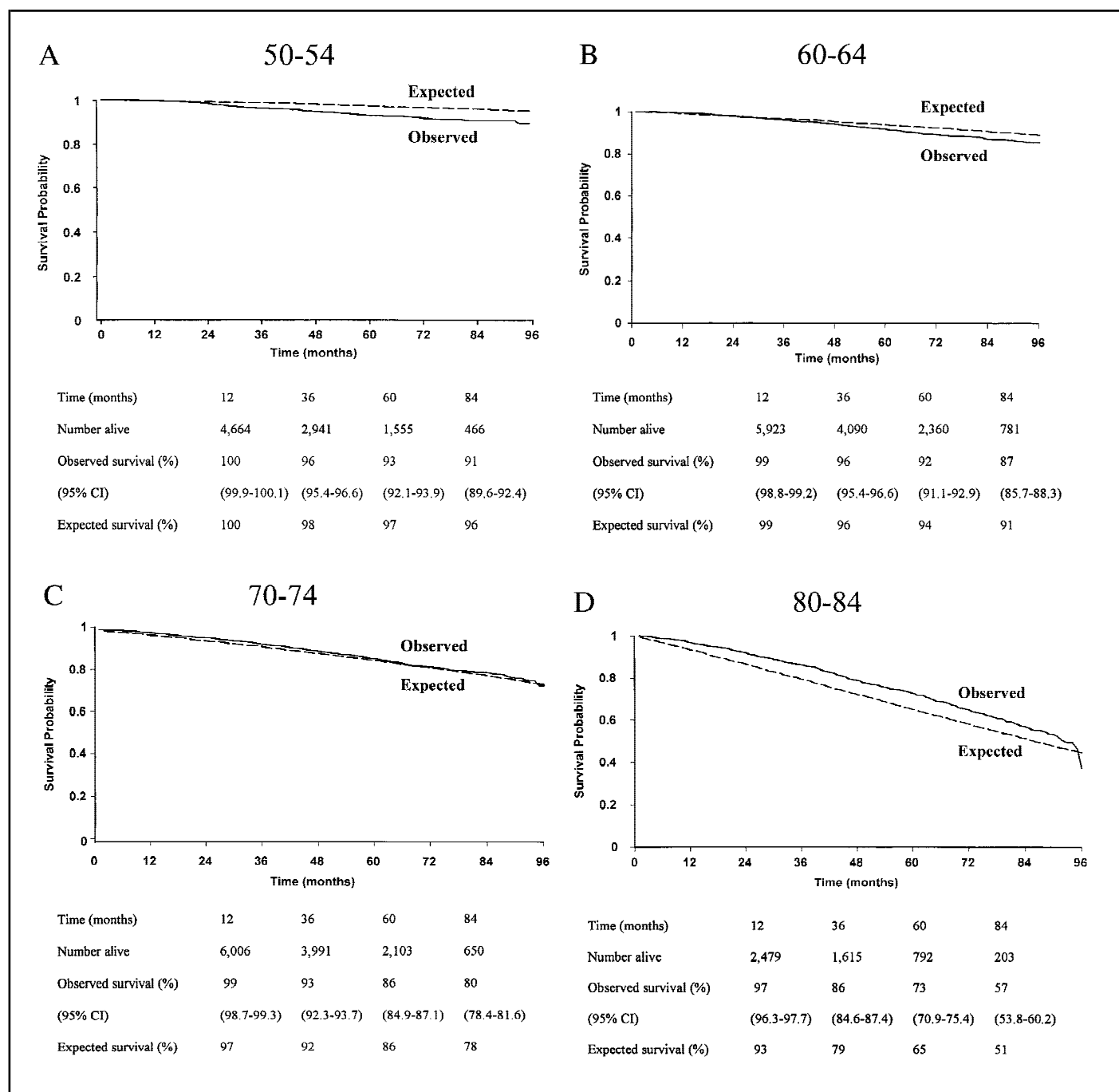


Fig. 1. Observed (solid lines) and expected (dashed lines) survivals in patients with lymph node-negative disease according to age in the Surveillance, Epidemiology, and End Results (SEER) registry. **A)** 50–54 years old; **B)** 60–64 years old; **C)** 70–74 years old; and **D)** 80–84 years old. CI = confidence interval.

in this patient population with documentation of causes of death are definitely needed. Another implication of this study is that the approach to therapy in elderly patients should take into consideration the presence of other comorbid conditions. This study confirms the finding of another study that found that other causes of mortality assume a greater role in older patients (12). Clearly, there is a lack in our ability to incorporate specific comorbid conditions in decision-making. Hopefully, ongoing studies such as the Collaborative Study on Cancer and Comorbidity by the National Institute on Aging and the National Cancer Institute (37) that is looking at comorbidity in elderly patients will provide more insight into this problem.

Finally, several limitations of this study should be considered. First, because data on several of the biologic factors (p53, c-erbB2, and epidermal growth factor receptor status) were available on small numbers of patients, larger studies are needed to confirm our findings for p53, c-erbB2, and epidermal growth factor receptor. Another limitation of this study is that breast tumors were included in the San Antonio databases because they were sent to laboratories for biochemical steroid receptor assays and/or DNA flow cytometric analyses. This situation represents a potential selection bias because these assays cannot be performed on very small carcinomas. However, because older patients had larger tumors and because smaller tumors are expected

Table 4. Breast cancer mortality in relation to all causes of mortality for all patients and patients with tumors smaller than 1 cm

Age group, y	All patients			Patients with tumors <1 cm		
	All causes, No.	Breast cancer, No.	%	All causes, No.	Breast cancer, No.	%
50–54	9555	7009	73	52	26	50
55–59	12 251	8227	67	79	30	38
60–64	14 306	8359	58	120	40	33
65–69	15 732	7884	50	205	49	24
70–74	15 902	6623	42	276	59	21
75–79	15 116	5138	34	290	36	12
80–84	12 130	3733	31	206	28	14
≥85	12 273	3540	29	160	25	16

to have more favorable biologic characteristics, perhaps the already favorable biologic characteristics of these carcinomas in the elderly would have been even better if more patients with very small tumors had been included. Finally, although this study is large, the databases used might not perfectly represent the population at large (38), and generalizing the findings from these databases to the general population should be done with caution.

REFERENCES

- (1) Statistical abstract of the United States. Washington (DC): U.S. Bureau of the Census; 1997.
- (2) Yancik R. Cancer burden in the aged: an epidemiologic and demographic overview. *Cancer* 1997;80:1273–83.
- (3) Landis SH, Murray T, Bolden S, Wingo PA. Cancer statistics, 1998 [published errata appear in *CA Cancer J Clin* 1998;48:192 and 1998;48:329]. *CA Cancer J Clin* 1998;48:6–29.
- (4) Surveillance, Epidemiology, and End Results (SEER) Program: Public use CD-ROM (1973–1995). Bethesda (MD): Cancer Statistics Branch, National Cancer Institute; 1998.
- (5) Goodwin JS, Hunt WC, Humble CG, Key CR, Samet JM. Cancer treatment protocols. Who gets chosen? *Arch Intern Med* 1988;148:2258–60.
- (6) Bergman L, Kluck HM, van Leeuwen FE, Crommelin MA, Dekker G, Hart AA, et al. The influence of age on treatment choice and survival of elderly breast cancer patients in south-eastern Netherlands: a population-based study. *Eur J Cancer* 1992;147:5–80.
- (7) de Rijke JM, Schouten LJ, Schouten HC, Jager JJ, Koppejan AG, van den Brandt PA. Age-specific differences in the diagnostics and treatment of cancer patients aged 50 years and older in the province of Limburg, The Netherlands. *Ann Oncol* 1996;7:677–85.
- (8) Goodwin JS, Hunt WC, Samet JM. Determinants of cancer therapy in elderly patients. *Cancer* 1993;72:594–601.
- (9) Yancik R, Ries LG, Yates JW. Breast cancer in aging women. A population-based study of contrasts in stage, surgery, and survival. *Cancer* 1989; 63:976–81.
- (10) Silliman RA, Guadagnoli E, Weitberg AB, Mor V. Age as a predictor of diagnostic and initial treatment intensity in newly diagnosed breast cancer patients. *J Gerontol* 1989;44:M46–50.
- (11) Clark GM. The biology of breast cancer in older women. *J Gerontol* 1992;47 Spec No:19–23.
- (12) Satariano WA, Ragland DR. The effect of comorbidity on 3-year survival of women with primary breast cancer. *Ann Intern Med* 1994;120: 104–10.
- (13) Newschaffer CJ, Bush TL, Penberthy LE, Bellantoni M, Helzlsouer K, Diener-West M. Does comorbid disease interact with cancer? An epidemiologic analysis of mortality in a cohort of elderly breast cancer patients. *J Gerontol A Biol Sci Med Sci* 1998;53:M372–8.
- (14) Yancik R, Havlik RJ, Wesley MN, Ries L, Long S, Rossi WK, et al. Cancer and comorbidity in older patients: a descriptive profile. *Ann Epidemiol* 1996;6:399–412.
- (15) Clark GM, Dressler LG, Owens MA, Pounds G, Oldaker T, McGuire WL. Prediction of relapse or survival in patients with node-negative breast cancer by DNA flow cytometry. *N Engl J Med* 1989;320:627–33.
- (16) Wenger CR, Beardslee S, Owens MA, Pounds G, Oldaker T, Vendely P, et al. DNA ploidy, S-phase, and steroid receptors in more than 127,000 breast cancer patients. *Breast Cancer Res Treat* 1993;28:9–20.
- (17) Clark GM, Wenger CR, Beardslee S, Owens MA, Pounds G, Oldaker T, et al. How to integrate steroid hormone receptor, flow cytometric, and other prognostic information in regard to primary breast cancer. *Cancer* 1993; 71:2157–62.
- (18) Ciocca DR, Fujimura FK, Tandon AK, Clark GM, Mark C, Lee-Chen GJ, et al. Correlation of HER-2/neu amplification with expression and with other prognostic factors in 1103 breast cancers. *J Natl Cancer Inst* 1992; 84:1279–82.
- (19) Clark GM, Osborne CK, Levitt D, Wu F, Kim NW. Telomerase activity and survival of patients with node-positive breast cancer. *J Natl Cancer Inst* 1997;89:1874–81.
- (20) Allred DC, Clark GM, Elledge R, Fuqua SA, Brown RW, Chamness GC, et al. Association of p53 protein expression with tumor cell proliferation rate and clinical outcome in node-negative breast cancer. *J Natl Cancer Inst* 1993;85:200–6.
- (21) Kaplan EL, Meier PL. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457–81.
- (22) Vital statistics of the United States, 1994 life tables, vol II. Hyattsville (MD): National Center for Health Statistics; March 1998.
- (23) The International Classification of Diseases, 9th revision. 3rd ed. Washington (DC): Department of Health and Human Services; March 1989.
- (24) Worden JK, Costanza MC, Foster RS Jr, Lang SP, Tidd CA. Content and context in health education: persuading women to perform breast self-examination. *Prev Med* 1983;12:331–9.
- (25) Zapka JG, Stoddard AM, Costanza ME, Greene HL. Breast cancer screening by mammography: utilization and associated factors. *Am J Public Health* 1989;79:1499–502.
- (26) Screening mammography: a missed clinical opportunity? Results of the NCI Breast Cancer Screening Consortium and National Health Interview Survey Studies. *JAMA* 1990;264:54–8.
- (27) Fisher B, Redmond C, Poisson R, Margolese R, Wolmark N, Wickerham L, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer [published erratum appears in *N Engl J Med* 1994;330:1467]. *N Engl J Med* 1989;320:822–8.
- (28) Veronesi U, Salvadori B, Luini A, Greco M, Saccocci R, del Vecchio M, et al. Breast conservation is a safe method in patients with small cancer of the breast. Long-term results of three randomised trials on 1,973 patients. *Eur J Cancer* 1995;31A:1574–9.
- (29) Overgaard M, Hansen PS, Overgaard J, Rose C, Andersson M, Bach F, et al. Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. Danish Breast Cancer Cooperative Group 826 Trial. *N Engl J Med* 1997;337:949–55.
- (30) Ragaz J, Jackson SM, Le N, Plenderleith IH, Spinelli JJ, Basco VE, et al. Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med* 1997;337:956–62.
- (31) Early Breast Cancer Trialists' Group. Polychemotherapy for early breast cancer: an overview of the randomised trials. *Lancet* 1998;352:930–42.
- (32) Adami HO, Walker B, Holmberg L, Persson I, Stone B. The relation between survival and age at diagnosis in breast cancer. *N Engl J Med* 1986;315:559–63.
- (33) Kerlikowske K, Grady D, Rubin SM, Sandrock C, Ernster VL. Efficacy of screening mammography, a meta-analysis. *JAMA* 1995;273:149–54.
- (34) Smith-Bindman R, Kerlikowske K. Is there a downside to elderly women undergoing screening mammography? [editorial]. *J Natl Cancer Inst* 1998; 90:1322–3.
- (35) Lerman C, Trock B, Rimer BK, Boyce A, Jepson C, Engstrom PF. Psychological and behavioral implications of abnormal mammograms. *Ann Intern Med* 1991;114:657–61.
- (36) Lerman C, Trock B, Rimer BK, Jepson C, Brody D, Boyce A. Psychological side effects of breast cancer screening. *Health Psychol* 1991;10: 259–67.
- (37) Havlik RJ, Yancik R, Long S, Ries L, Edwards B. The National Institute on Aging and the National Cancer Institute SEER collaborative study on co-

morbidity and early diagnosis of cancer in the elderly. *Cancer* 1994;74: 2101–6.

- (38) Frey CM, McMillen MM, Cowan CD, Horm JW, Kessler LG. Representativeness of the Surveillance, Epidemiology, and End Results Program data: recent trends in cancer mortality rates. *J Natl Cancer Inst* 1992;84: 872–7.

NOTES

¹*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit orga-

nizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

Supported by Public Health Service Medical Oncology Program Project grant CA30195, Specialized Program of Research Excellence grant CA58183-02, and grant P30CA54174 (to the San Antonio Cancer Institute) from the National Cancer Institute, National Institutes of Health, Department of Health and Human Services.

Manuscript received July 22, 1999; revised December 17, 1999; accepted January 5, 2000.