

# Effect of Age and Comorbidity in Postmenopausal Breast Cancer Patients Aged 55 Years and Older

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**B**REAST CANCER IS THE LEADING contributor to cancer incidence among women in the United States.<sup>1</sup> This tumor ranks second after lung cancer as a cause of cancer deaths among women.<sup>1</sup> A total of 192 200 new cases and 40 200 deaths are estimated for 2001.<sup>2</sup> The brunt of this high number of breast cancer cases and deaths is borne by women in the postmenopausal period of life, defined herein as age 55 years and older. Two thirds of all newly diagnosed female breast cancer patients are in this age group.<sup>1</sup> The peak incidence rates, more than 400.0 per 100 000 population, occur in women aged 70 to 74 years (461.5), 75 to 79 years (482.3), and 80 to 84 years (472.9). Women aged 85 years and older have an incidence rate of 394.0 per 100 000 population.<sup>1</sup> Of deaths due to breast cancer, 77% occur in patients aged 55 years and older.<sup>1</sup> There is an escalation of mortality rates with each successive 5-year age group with the highest rate, 200.4 per 100 000 population, occurring in the 85-years-and-older age group.<sup>1</sup>

Concurrent with an increased vulnerability to breast cancer, increasing

**Context** Postmenopausal women aged 55 years and older have 66% of incident breast tumors and experience 77% of breast cancer mortality, but other age-related health problems may affect tumor prognosis and treatment decisions.

**Objective** To document the comorbidity burden of postmenopausal breast cancer patients and evaluate its relationship with age on disease stage, treatment, and early mortality.

**Design and Setting** Data were collected on breast cancer patients' comorbidities by retrospective hospital medical records review and merged with information on patients' tumor characteristics collected from 6 regional National Cancer Institute Surveillance, Epidemiology, and End Results cancer registries. Patients were followed up until death or for 30 months from breast cancer diagnosis.

**Participants** Population-based random sample of 1800 postmenopausal breast cancer patients diagnosed in 1992 stratified by 3 age groups: 55 to 64 years, 65 to 74 years, and 75 years and older.

**Main Outcome Measures** Extent of disease, therapy received, comorbidity, cause of death, and survival.

**Results** Seventy-three percent (1312 of 1800) of the sample was diagnosed with stage I and II breast cancer, 10% (n=188) with stage III and IV breast cancer, and 17% (n=300) did not have a stage assignment. Of the 1017 patients with stage I and stage II node-negative breast cancer, 95% received therapy in agreement with the National Institutes of Health consensus statement recommendation for early-stage breast cancer. Patients in older age groups were less likely to receive therapy consistent with the consensus statement ( $P<.001$ ), and women aged 70 years and older were significantly less likely to receive axillary lymph node dissection as determined by logistic regression analysis ( $P<.01$ ). Diabetes, renal failure, stroke, liver disease, a previous malignant tumor, and smoking were significant in predicting early mortality in a statistical model that included age and disease stage. Breast cancer was the underlying cause of death for 135 decedents (51.3%). Heart disease (n=45, 17.1%) and previous cancers (n=22, 8.4%) were the next major underlying causes. In the 30-month follow-up period, 263 patients (15%) died.

**Conclusion** Patient care decisions occur in the context of breast cancer and other age-related conditions. Comorbidity in older patients may limit the ability to obtain prognostic information (ie, axillary lymph node dissection), tends to minimize treatment options (eg, breast-conserving therapy), and increases the risk of death from causes other than breast cancer.

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age also confers high risks for a number of other health problems.<sup>3,4</sup> Postmenopausal breast cancer patients frequently have 1 or more preexisting

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comorbid conditions at the time of diagnosis (eg, heart disease, chronic obstructive pulmonary disease, diabetes, hypertension, and arthritis).<sup>5-8</sup> Thus, the prediagnostic health status of breast cancer patients in middle and later age groups may affect tumor prognosis and treatment decisions. Studies have shown that age and comorbidity strongly influence therapeutic decisions and are associated with less aggressive cancer therapy<sup>7-19</sup> and that older women are less likely to have an extensive pretreatment assessment.<sup>8,13,16-18</sup> In studies of postmenopausal women diagnosed with breast cancer, the effects of aging and the increased likelihood of concomitant comorbidity should be taken into account.<sup>13-15,19</sup> Another crucial area for research on older women with breast cancer is in the evaluation of therapies in clinical trials. Much of the data on cancer treatment efficacy comes from clinical trial investigations that tend to exclude breast cancer patients aged 70 years and older who are likely to have preexisting diseases and other health limitations.<sup>20,21</sup>

The complex clinical situation of aging and comorbidity in postmenopausal breast cancer patients is illustrated in analyses conducted by the National Institute on Aging (NIA) Epidemiology, Demography, and Biometry and National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) Programs.<sup>6,22</sup> This article describes the comorbidity burden of postmenopausal breast cancer patients, investigates the relationship of comorbidity to age and tumor stage, assesses the effect of comorbidity on initial surgical treatment of breast cancer, and evaluates the impact of comorbidity on survival in the 30 months following diagnosis.

## METHODS

Women diagnosed with breast cancer between January 1, 1992, and December 31, 1992, were randomly selected within tumor registry and age stratum to achieve approximately equal sample sizes in 3 age groups: 55 to 64 years,

65 to 74 years, and 75 years and older. Six SEER registries (Iowa; New Mexico; Utah; San Francisco-Oakland, Calif; Atlanta, Ga; and Seattle, Wash) participated in the study. The comorbidity data were collected as a special study in addition to those tumor registry data routinely obtained as part of the NCI SEER Program (eg, histology, extent of disease, first course of treatment, and vital status). General methods for the NIA/NCI Study have been described in detail.<sup>6,22</sup> Physician notes, anesthesia notes, nursing notes, discharge summaries, and reports from radiology and various laboratories provided the greatest share of the information.

For this analysis, the comorbid conditions present were classified as category 1: current medical management or diagnostic problem; or category 2: not a current problem. If whether the comorbid condition was concurrent with the tumor diagnosis could not be determined, the comorbidity was assumed to be not a current problem (category 2). The presence of comorbidity refers to the "current management" (category 1) unless otherwise specified. In addition, a set of comorbidities was designated as "high severity" disease. These comorbidities are chronic obstructive pulmonary disease (both categories 1 and 2); diabetes requiring insulin; high-severity heart disease such as cardiac arrest, congestive heart failure (categories 1 and 2); current heart conditions such as angina, arrhythmia, cardiovascular disease, and myocardial infarction (category 1); previous malignant cancer; and renal failure (categories 1 and 2).

Staging was done using the American Joint Committee on Cancer classification system.<sup>23</sup> Patients lacking sufficient stage information are classified as "stage unknown." Surgical and radiation therapies, administered or planned, during the initial treatment interval (up to 4 months) are collected by SEER registries. Data for early-stage breast cancer patients were analyzed. Data on survival were obtained through the SEER Program. More than 99% of the patients were followed up to death or were

still alive at the end of the 30-month postdiagnosis period used in this study. Data for 1 patient were not included in the survival analysis because time to death could not be determined.

The Mantel-Haenszel trend test was used to compare ordered categorical variables. Logistic and Cox regression models controlled for the sampling age groups.<sup>24-28</sup> Statistical tests were performed against 2-sided alternatives. Unless otherwise stated, a level of  $P < .05$  was used to determine statistical significance. The SAS system was used to perform analyses (SAS System, release 6.12; SAS Institute Inc, Cary, NC).

## RESULTS

### Age and Tumor Characteristics

The age range in the sample of 1800 patients was 55 to 101 years. Ninety-three percent of the patients were white (of whom 5% were reported as Hispanic), 5% were black, and 2% were other races. The number of patients in the age-stratified samples was 622, 624, and 554 in the 55-to-64-year, 65-to-74-year and 75-years-and-older age groups, respectively. A subset of 127 patients aged 85 years and older was used in some analyses. Details are also provided on 5-year age-specific groups between 55 and 84 years and 85 years and older when possible.

Eighty-two percent of the patients had infiltrating ductal carcinoma and 8% had lobular carcinoma. Histology for the remaining 10% of patients included mucin-producing adenocarcinoma, subtypes of signet-ring cell carcinoma, medullary, papillary, Paget, and inflammatory carcinomas. The 1992 breast cancer diagnosis was the first tumor recorded in the SEER database for 85% of the patient sample. For 13% of the patient sample, this was a second diagnosis of a primary malignancy; for 2% of patients, it was the third or fourth primary cancer recorded in the SEER registry.

### Age, Disease Stage, Treatment, and Mortality

The stage distribution of the NIA/NCI SEER Study breast cancer patient cohort by 5-year age groups and age 85

years and older is shown in FIGURE 1. Almost three quarters (n=1312) of the sample was diagnosed with stage I (n=807) and II (node negative, n=210; node positive, n=295); 10% (n=188) was diagnosed with stage III and IV disease. A high proportion of patients (n=300) did not have a stage assignment.

The percentage of patients for whom the stage was unknown was associated with increasing age with an average of 11% for women in the 3 youngest 5-year postmenopausal age groups to 16%, 18%, and 22%, respectively, for women in the 3 older age groups. In patients aged 85 years and older, the percentage increases to slightly more than 50%. Inability to assign a stage was due to insufficient data on nodal, primary, and/or metastatic tumor status.

### Therapy

According to the NIH Consensus Statement for Treatment of Early Stage Breast Cancer (ie, stage I and stage II node-negative breast cancer), the recommended therapy for stage I and stage II node-negative breast cancer is defined as either a partial mastectomy and radiation (ie, breast-conservation therapy) or a modified radical mastectomy.<sup>29</sup> Of the 1017 patients so classified, 95% received therapy in agreement with the consensus statement recommendation. Adjusted for disease stage, patients in older age groups were less likely to receive therapy consistent with the consensus statement ( $P<.001$ ) (TABLE 1).

In patients classified as having early-stage disease who received partial mastectomies, older patients received

radiation therapy less frequently ( $P<.001$ ). Multivariate modeling with age group and stage showed that patients with stage II disease were more likely to receive radiation therapy than patients with stage I disease.

### Prognostic Evaluation

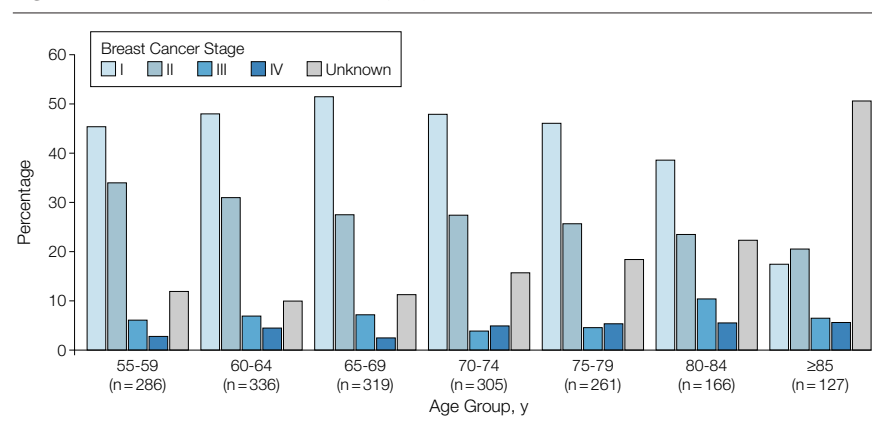
The relationship between age group and a known disease stage (FIGURE 2A) is highly significant ( $P<.001$ ). Fewer axillary lymph node dissections (AxLND) were performed in women aged 70 years and older, which accounts for the high proportion of the older patients whose tumors were classified as stage unknown.

We investigated the frequency of initial surgical treatment that included AxLND in women without obvious advanced disease (ie, stages IIIB and IV). In a logistic regression model with the size of the primary tumor as a covariate, age group was a significant determinant for receiving an AxLND. Women in the 5-year groups starting at age 70 years were significantly less

likely to undergo this procedure compared with the youngest age group ( $P<.001$  for Wald  $\chi^2$  test). When individually added to the model containing age and tumor size, diabetes requiring insulin, stroke, gastrointestinal tract problems, mental health problems, and a previous malignant tumor were significant in predicting that the patient was less likely to receive an AxLND. Age group and tumor size remained significant in each model.

Multivariate models including these significant comorbidities did not alter the odds ratios for age by more than 5% and did not change the trend of less AxLND with increasing age. Including the significant comorbidities in the model changed the odds ratio for the oldest age group ( $>85$  years) by less than 1%. Paradoxically, when an AxLND was performed in older women, they tended not to receive breast-conserving surgery (Figure 2B). A comparison of patients in whom a partial mastectomy with AxLND was performed vs treatment with a modified

**Figure 1.** Stage Distribution of Cancer by Age

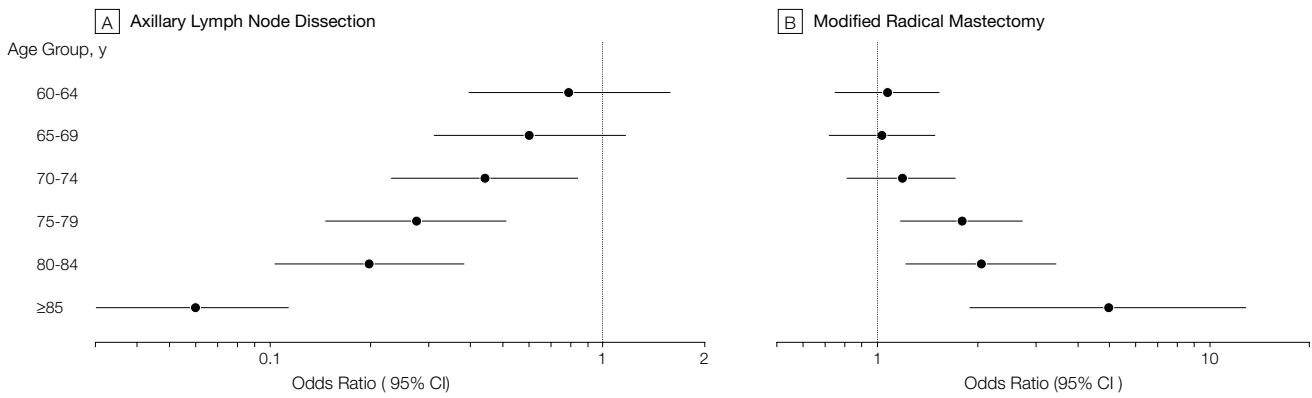


**Table 1.** Cancer Therapy in Patients With Stage I and Stage II Node-Negative (Early-Stage) Breast Cancer by Age\*

Therapy	Age, y							Total
	55-59	60-64	65-69	70-74	75-79	80-84	≥85	
Modified radical mastectomy	97 (57.7)	123 (60.6)	117 (59.1)	113 (63.1)	111 (73.5)	60 (72.3)	30 (85.7)	651 (64.0)
Partial mastectomy and radiation therapy	68 (40.5)	75 (37.0)	74 (37.4)	56 (31.3)	29 (19.2)	14 (16.9)	3 (8.6)	319 (31.4)
Less than minimum expected therapy	3 (1.8)	5 (2.5)	7 (3.5)	10 (5.6)	11 (7.3)	9 (10.8)	2 (5.7)	47 (4.6)
<b>Total</b>	<b>168</b>	<b>203</b>	<b>198</b>	<b>179</b>	<b>151</b>	<b>83</b>	<b>35</b>	<b>1017</b>

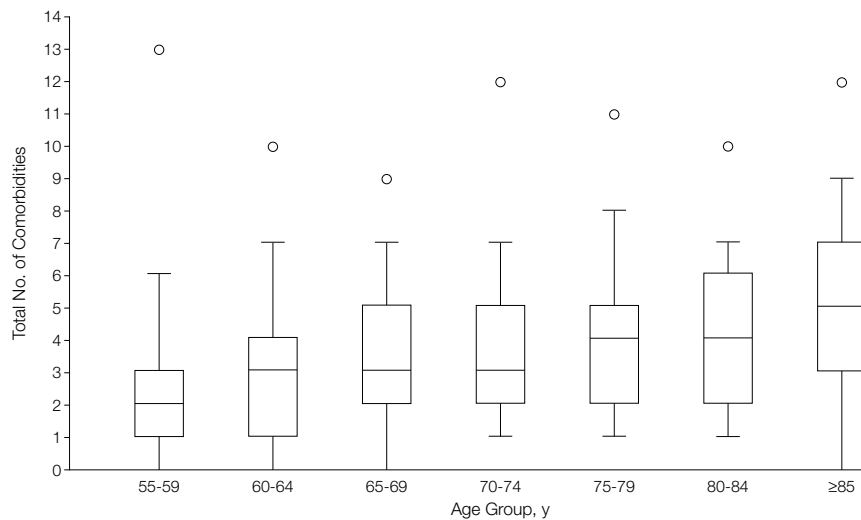
\*Data are presented as No. (%) unless otherwise indicated.

**Figure 2.** Distribution of Axillary Lymph Node Dissection and Modified Radical Mastectomy by Age



CI indicates confidence interval.

**Figure 3.** Distribution of Total Number of Comorbidities by Age



Box indicates the 25th to 75th percentiles; horizontal line inside box, the median; whiskers, 5th and 95th percentiles; and open circles, maximum. The minimum in all groups is 0.

radical mastectomy revealed that women in the older age groups were more likely to receive the more extensive surgery. Adjusting for stage, an increase with advancing age was seen in the estimated odds of receiving a modified radical vs a partial mastectomy with AxLND.

**No Surgery**

Seventy patients did not undergo surgical therapy. Forty-five stage III or IV breast cancer patients may not have required surgery either for staging or as

a primary therapy; 25 patients were unstaged, of whom 12 were aged 85 years or older. The unstaged patients did not receive surgical therapy because the patient refused, surgery was not recommended, or surgery was contraindicated. Sixty-eight percent of these patients died within the 30-month post-diagnosis period. The median survival within the follow-up period for these unstaged patients was 17 months. Unstaged patients 85 years and older who did not receive surgery tended to have more severe comorbidities than pa-

tients in this age group who received surgery. However, the trend was not statistically significant.

**Comorbidity**

The number of comorbidities per individual patient ranged from none to 13. Seven percent of patients had no comorbidities recorded, 49% had 1 to 3, 34% had 4 to 6, and 9% had 7 to 13. The total number of comorbidities increased with age ( $P < .001$ ), as shown in FIGURE 3. Not surprisingly, the percentage of patients with “high-severity” comorbidities also increased with age ( $P < .001$ ).

The distribution of conditions varied considerably by age group because the age range for the breast cancer patient sample was 55 to 101 years. Some comorbidities characteristically occur in middle age or earlier; others occur at older ages. Some comorbidities may be etiologically related to the tumor, while others are age-related and chronic, but not necessarily disabling. Major illnesses (eg, cancer, heart problems, and diabetes requiring insulin or conditions related to these diseases) may also be concurrent. FIGURE 4 shows these variations for selected common prevalent conditions.

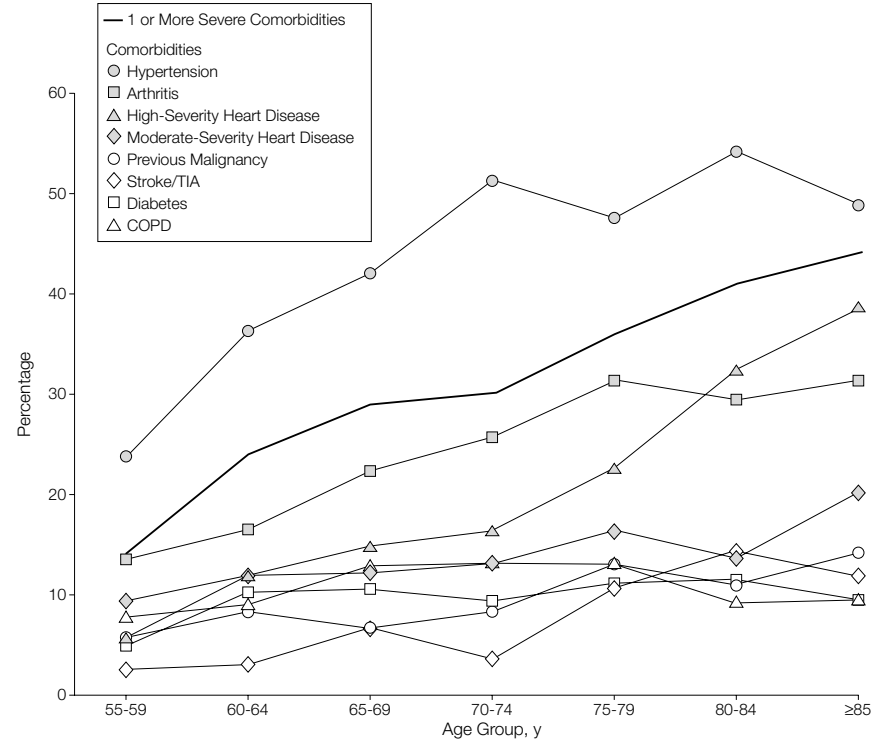
The most prevalent condition in all age groups was hypertension. Arthritis ranked second or third across all age groups. High-severity heart disease (defined in the “Methods” section) af-

ected less than 6% of patients aged 55 to 59 years, but increased to second or third in comorbidity prevalence for the 4 oldest age groups (16.4%, 22.6%, 32.5%, and 38.6% for age groups 70 to 74 years, 75 to 79 years, 80 to 84 years, and 85 years and older, respectively). The percentage of patients with 1 or more severe comorbidities tended to increase with each successive age group. All trends shown in Figure 4 are statistically significant with the exception of diabetes and chronic obstructive pulmonary disease. Other comorbidities in which prevalence increased significantly with age were eye problems, anemia, depression, fractures, hearing problems, osteoporosis, Parkinson disease, renal failure, and low-severity urinary tract problems. The percentage of current smokers decreased significantly with increasing age. For patients with an assigned disease stage, the classification was not influenced by comorbidity. After adjusting for age group, no significant relationship of disease stage with total number of comorbidities or the number of highly severe or moderately severe comorbidities was found. Neither was there a significant relationship of comorbid conditions to the likelihood of having an unknown stage.

### Previous Cancers

The proportion of patients with previous cancers increased by age: 11% for those aged 55 to 64 years, 14% for those aged 65 to 74 years, and 20% for patients aged 75 years and older. Fifteen percent (n=268) of the breast cancer patients had 1 or more previous cancers recorded in the SEER database for a total of 301 cancers. Anatomic site was recorded for 64% previous cancers. Malignancies of the breast (42%), corpus uteri (14%), colon and rectum (14%), melanomas (5%), cervix (4%), and ovary (3%) accounted for more than four fifths of the antecedent tumors with known anatomic sites. The remaining cancers included leukemia, non-Hodgkin lymphoma, and cancers of lung, bladder, and other sites.

**Figure 4.** Prevalence and Age Trends by Selected Comorbidities



TIA indicates transient ischemic attack; COPD, chronic obstructive pulmonary disease. All trends were significant at the  $P < .05$  level except for diabetes and COPD.

### Survival

Age group was a statistically significant determinant of decreased survival in disease stages I ( $P = .007$ ) and II ( $P < .001$ ) and unknown stage ( $P < .001$ ). In disease stages III and IV, age group was not a statistically significant determinant of survival. The effect of comorbidity on survival was explored using multivariate models that adjusted for age group and stage. Each covariate was added separately to a model containing age group and disease stage. Covariates that added significantly to the model ( $P < .10$ ) were entered into a backward selection procedure. Age group and stage were forced into the model. Covariates that remained after backward selection, their risk ratios, and 95% confidence intervals are shown in TABLE 2.

Advanced disease stage, older age, and presence of certain specific comorbidities are associated with a higher risk of dying. Patients with stage III disease were

at an 8-fold greater risk than stage I patients. Stage IV patients had a 27-fold increased risk. Women aged 75 years and older had a greater than 2-fold excess risk compared with the youngest age group (55-64 years); there was no significant difference between the 2 younger age groups (55-64 and 65-74 years). Renal failure (acute and chronic), liver disease, and stroke or transient ischemic attack increased the risk ratio by 2-fold or greater compared with patients without these comorbidities.

### Cause of Death

In the 30-month postdiagnosis period, 15% (n=263) of the patients had died (TABLE 3). Fifty-one percent (n=135) of the total deaths occurring within 30 months were attributed to breast cancer. The percentage of deaths ascribed to breast cancer decreased with age.

In the 2 oldest age groups, 75 to 84 years and age 85 years and older, fewer



than half the deaths in the 30-month period were due to breast cancer. The proportion of patients dying and the causes of death were similar for the age groups 55 to 64 years and 65 to 74 years. Approximately 10% of the patients in these 2 age groups died within 30 months of diagnosis. In the older age groups (75-84 years and age 85 years and older), the percentages of patients

who died were much higher: 20% and 46%, respectively.

Other cancers and concomitant health problems accounted for a greater proportion of deaths in patients aged 75 years and older. Overall, 8.4% (n=22) died of malignancies other than breast cancer (metastases or another primary tumor). With advancing age, heart and cerebrovascular diseases became increasingly important as causes of death.

**Table 2.** Multivariate Model of 30-Month Survival by Age, Cancer Stage, and Comorbidity

Covariate	Risk Ratio (95% Confidence Interval)
Age group, y	
55-64 (reference)	1.00
65-74	0.89 (0.61-1.28)
≥75	2.46 (1.80-3.36)
Stage	
Stage I (reference)	1.00
Stage II	2.32 (1.56-3.44)
Stage III	8.27 (5.33-12.85)
Stage IV	26.55 (17.48-40.31)
Stage unknown	3.58 (2.42-5.31)
Dichotomous variables*	
Renal failure (current/history)	3.30 (1.44-7.54)
Liver disease	2.87 (1.24-6.65)
Stroke/transient ischemic attack	2.30 (1.21-4.37)
Asthma	1.98 (1.06-3.73)
Diabetes	1.76 (1.23-2.52)
Previous malignant cancer (current/history)	1.57 (1.12-2.20)
Smoking	1.54 (1.07-2.23)
Chronic obstructive pulmonary disease	1.49 (1.01-2.17)
Hypertension	0.77 (0.60-1.00)
Arthritis	0.66 (0.48-0.91)
Lipid problems	0.23 (0.07-0.77)

\*Reference group is the group without the characteristic.

## COMMENT

Age and comorbidity limit diagnostic tests and examinations, narrow treatment choices, and are associated with risk of early mortality in postmenopausal women with breast cancer. This was particularly apparent for elderly postmenopausal patients (ie, aged 70 years and older). Older patients were less likely to have an AxLND and were less likely to receive the therapy recommended by the 1990 National Institutes of Health Consensus Development Conference on Treatment of Patients with Early Stage Invasive Breast Cancer<sup>29</sup> for early-stage disease. Older patients with early-stage disease who received partial mastectomies were less likely to receive radiation therapy. The total number of comorbidities reported increased by age group. In our study's 30-month follow-up period, concurrent health problems and other cancers (another tumor or metastases to a different cancer site) accounted for a greater proportion of

deaths than breast cancer in patients aged 75 years and older.

Older women were more likely to have their breast cancer classified as unknown stage. This may have been due to a presumed inability to tolerate surgery because of other health problems and also could have increased the likelihood of receiving less than optimal therapy. Almost two thirds of the patients with unknown stage disease were aged 70 years and older. The compromised health status of elderly postmenopausal breast cancer patients quite likely precludes obtaining certain prognostic information (ie, AxLND), and minimizes the treatment options that may be offered by the physician or accepted by the patient. Poor health status may even interact with the breast malignancy and its treatment, possibly increasing the severity of other conditions and the risk of death from causes other than breast cancer. Finally, treatment alternatives may be limited by the comorbidity resulting in less aggressive therapy at the outset.

For women with stages I and II node-negative breast cancer, the older the patient, the less likely she was to have received an AxLND. Patients aged 75 years and older, without obvious advanced disease, received an AxLND less frequently than younger patients, thus resulting in a greater number of the oldest patients with unknown disease stage classification. Possible explanations for the large number of patients (n=300) in this category are that the axillary lymph nodes may have been assessed clinically negative by the physician; the patient may have been too ill to tolerate this procedure; the patient was unable to provide informed consent; the physician chose not to offer this option; the patient did not want an AxLND; and the family did not want the patient to have an AxLND. These findings are consistent with those from previous studies and reports<sup>7-19,30-34</sup> indicating that age is associated with more conservative cancer diagnostic and prognostic evaluations.

With a shift toward smaller breast cancers as a result of more mammography screening in the latter half of the 1980s and early 1990s,<sup>2</sup> increasing

**Table 3.** Cause of Death According to Age Group\*

	Age, y				Total
	55-64	65-74	75-84	≥85	
Breast cancer	48 (75.0)	33 (58.9)	38 (44.7)	16 (27.6)	135 (51.3)
Other cancer	4 (6.2)	6 (10.7)	9 (10.6)	3 (5.2)	22 (8.4)
Heart disease	4 (6.2)	4 (7.1)	18 (21.2)	19 (32.8)	45 (17.1)
Cerebrovascular disease	0	1 (1.8)	4 (4.7)	8 (13.8)	13 (4.9)
Digestive system	1 (1.6)	1 (1.8)	3 (3.5)	4 (6.9)	9 (3.4)
Alzheimer disease/dementia	1 (1.6)	0	4 (4.7)	2 (3.4)	7 (2.7)
Pneumonia	0	0	2 (2.4)	3 (5.2)	5 (1.9)
COPD/other respiratory	1 (1.6)	2 (3.6)	1 (1.2)	1 (1.7)	5 (1.9)
Other	5 (7.8)	4 (7.1)	2 (2.4)	2 (3.4)	13 (4.9)
Unknown	0	5 (8.9)	4 (4.7)	0	9 (3.4)
<b>Total No. of Deaths</b>	<b>64</b>	<b>56</b>	<b>85</b>	<b>58</b>	<b>263</b>
<b>Total No. of Patients</b>	<b>622</b>	<b>624</b>	<b>427</b>	<b>127</b>	<b>1800</b>

\*COPD indicates chronic obstructive pulmonary disease. Data are presented as No. (%) unless otherwise indicated.

numbers of clinicians believed that AxLND was unnecessary for patient management decisions not dependent on axillary lymph node status.<sup>35-39</sup> A trend of not receiving AxLND was documented in a large study of 84 178 patients with local-stage breast cancer.<sup>40</sup> The likelihood of not receiving AxLND significantly increased from 1983-1987 to 1988-1993.<sup>40</sup> Unmarried, nonwhite, and older women were less likely to have received AxLNDs.<sup>40</sup>

Certain comorbidities (eg, diabetes requiring insulin, stroke, gastrointestinal tract problems, mental health problems, and a previous malignancy) were found to be significant predictors of nonreceipt of the AxLND in women without obvious advanced disease. However, adjusting for the presence of 1 or more of these comorbidities did not explain the tendency for elderly patients to receive an AxLND less frequently than younger patients. There could have been concern about the procedure's potential morbidity in older patients.<sup>41</sup> Almost half of the patients classified as stage unknown who did not receive surgery were aged 85 years and older (12 of 25 patients). The small sample size prohibits extensive statistical modeling, but it is notable that 68% of these patients were dead within the 30-month follow-up.

Stage of disease is a strong prognostic indicator of survival for breast cancer patients as shown by the dramatically increasing risk ratios for disease stages II, III, and IV. Screening programs aimed at diagnosing breast cancers at lower stages would increase survival in women of all ages. Certain comorbidities contributed to an abbreviated survival. Many of these are more prevalent in the older age groups. Age group was a highly significant prognostic factor in stage I and II disease. The risk ratio for the oldest age group was significant in a multivariate model that included 11 specific comorbidities. These elderly patients are at risk not only because of the comorbidities present at the time of diagnosis but also may be at increased risk for exacerbation of their comorbidities concomitant with the diagnosis of cancer and for developing ad-

ditional comorbidities postdiagnosis. They also may be more physiologically vulnerable to treatment toxicity from the current or previous cancers (eg, less reserve capacity in renal function). Even with the individual comorbidities in the model, there was an additional explanatory effect of having 6 or more comorbidities. The impact of a multiple comorbidity burden may be more than that of the sum of the individual comorbidities. In disease stages III and IV, age was not a statistically significant determinant of survival in the first 30 months following diagnosis. For these patients, the tumor burden may override the effects of older age and concomitant comorbidities.

Our study has some limitations. Because of the retrospective medical record review approach, we could not include information on physical functioning of the patients prior or subsequent to hospitalization. The data obtained concerning medical procedures, while detailed, was confined to the hospital-based setting. The sample size was not sufficient to explore the confounding of age and increased comorbidity and the effect of these factors on survival, especially on the ability to assign a breast cancer disease stage.

The unique contribution of the NIA/NCI SEER study, however, is a comprehensive assessment of comorbidity, generalizability, and sustained follow-up of patient survival and mortality via a coordinated, quality-controlled record-keeping system in 6 state and regional population-based cancer registries active as NCI SEER registries since 1973. Our population-based infrastructure base contrasts with other comorbidity investigations that are single-registry, single-hospital, or multiple-hospital studies confined to a single area.

The NIA/NCI SEER study's strengths lie in acquisition of data on health problems recorded by physicians, nurses, and other health professionals as a routine part of patient evaluation in combination with data on breast cancer characteristics in a quality-controlled tumor registry record system. These data are more clinically precise than those obtained

from patient self-reports or administrative databases that use discharge data and *International Classification of Diseases, Ninth Revision (ICD-9)* codes with the inherent limitation that the patient would have required hospitalization for the comorbid condition. Data abstracters were specially trained SEER registry staff accustomed to working with medical records and tumor registry data. The abstracters' skillful probing of information allowed us to address a wide spectrum of comorbidities recorded for patients aged 55 years and older. Some studies use only a limited number of selected diseases as key conditions or rely on hospital-based mortality indices with 6 conditions. Our sample size permitted analysis of age subgroups within sampling strata and an opportunity to address breast cancer issues affecting women in their eighth and ninth decades of life as well as younger women to acquire a broader understanding of the effect of the comorbidity burden on breast cancer.

## CONCLUSIONS

Given the incidence of breast cancer in postmenopausal women, who may have other health problems, research is crucial to determine if treatment should differ according to age and health status. Given the heterogeneity of individuals within older age groups, age is not an appropriate criterion for breast treatment decisions.<sup>5,8,11-13,17-18,42</sup> Aging and comorbidity must be incorporated into the mainstream of breast cancer clinical research and in clinical trials to evaluate cancer treatment options for older women. Explicit attention should be directed to studies on effectiveness of AxLND and radiation therapy in patients in the eighth and ninth decades of life. The efficacy of less aggressive treatment strategies in older breast cancer patients, especially women aged 70 years and older, is an understudied area even though the highest rates of newly diagnosed breast cancer occur in this age group. In-depth studies must address the physiological ramifications of having certain comorbid conditions and breast cancer in tandem in women with advanced

age to ascertain their combined impact on the cancer trajectory. Guidelines for adjuvant chemotherapy, tamoxifen, or both in older breast cancer patients should be formulated on a firm foundation of clinical research. Drug behavior and response, optimal dose intensity, and schedules are poorly documented for the elderly population. Physicians must encourage screening and surveillance for breast cancer in postmenopausal women.

Breast cancer assumes even greater prominence as a public health concern with the aging of the "baby boom" generation of women. In the first 3 decades of this century, the proportion of older women (ie, aged 65 years and older) will increase from the current 14.5% to 21.3% in 2030.<sup>43</sup> Thus, even greater numbers of women in this age segment of the population will be vulnerable to breast cancer. As long as prevention and cure of breast cancer remain elusive, postmenopausal women will require additional health resources to promote early detection, optimum treatment, long-term follow-up, and supportive care.

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