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ORIGINAL REPORT

Breast Cancer Among the Oldest Old: Tumor Characteristics, Treatment Choices, and Survival

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ABSTRACT

Purpose
Few data are available on breast cancer characteristics, treatment, and survival for women age 80 years or older.

Patients and Methods
We used the linked Surveillance, Epidemiology and End Results-Medicare data set from 1992 to 2003 to examine tumor characteristics, treatments (mastectomy, breast-conserving surgery [BCS] with radiation therapy or alone, or no surgery), and outcomes of women age 80 years or older (80 to 84, 85 to 89, ≥ 90 years) with stage I/II breast cancer compared with younger women (age 67 to 79 years). We used Cox proportional hazard models to examine the impact of age on breast cancer–related and other causes of death. Analyses were performed within stage, adjusted for tumor and sociodemographic characteristics, treatments received, and comorbidities.

Results
In total, 49,616 women age 67 years or older with stage I/II disease were included. Tumor characteristics (grade, hormone receptivity) were similar across age groups. Treatment with BCS alone increased with age, especially after age 80. The risk of dying from breast cancer increased with age, significantly after age 80. For stage I disease, the adjusted hazard ratio of dying from breast cancer for women age ≥ 90 years compared with women age 67 to 69 years was 2.6 (range, 2.0 to 3.4). Types of treatments received were significantly associated with age and comorbidity, with age as the stronger predictor (26% of women age ≥ 80 years without comorbidity received BCS alone or no surgery compared with 6% of women age 67 to 79 years).

Conclusion
Women age ≥ 80 years have breast cancer characteristics similar to those of younger women yet receive less aggressive treatment and experience higher mortality from early-stage breast cancer. Future studies should focus on identifying tumor and patient characteristics to help target treatments to the oldest women most likely to benefit.

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INTRODUCTION

Women age 80 years and older are the fastest growing segment of the US population, and breast cancer is relatively common among these women with nearly 400 cases per 100,000 women.[1] Despite the high incidence, little is known about breast cancer characteristics, treatment choices, and survival among the oldest women. These data are important for decision making around breast cancer detection and care. Few randomized controlled trials that evaluated the effectiveness of breast cancer treatments included women age 80 years or older, and most observational studies were limited by small sample sizes in this age range.[2-4] Studies using the Surveillance, Epidemiology and End Results (SEER) -Medicare data set have examined the effectiveness of radiation treatment and chemotherapy among older women with breast cancer.[5-8] However, these studies consistently exclude women with missing stage and those without a histologic diagnosis and/or known hormonal receptivity. Meanwhile, women age 80 years or older are most likely to fall into these categories.[2,4,9-12] Missing data may be one reason that studies differ on whether elderly women present with higher stage disease but with less aggressive tumors than younger women.[2,13,14]

Although studies consistently show that older women are undertreated for breast cancer, the impact of undertreatment on breast cancer survival among older women remains controversial. Gadjos et al[3] found that rates of recurrence were not increased when undertreated women (older than 70 years) were compared with conventionally treated patients, while others have found that undertreatment is associated with recurrence and decreased survival.[2,15,16]

The purpose of this study was to examine variations in breast cancer tumor characteristics, initial treatments received, and survival among women age 80 to 84, 85 to 89, and ≥ 90 years with early-stage (stage I or II) breast cancer compared with younger women (age 67 to 79 years).

PATIENTS AND METHODS

We used data from the National Cancer Institute's linked SEER-Medicare data set. Since 1992, SEER has included 11 population-based tumor registries in the metropolitan areas of San Francisco/Oakland, Detroit, Atlanta, and Seattle; Los Angeles County; the San Jose–Monterey area; and the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii.[17] These areas cover approximately 14% of the US population.[18] We identified all women age 67 years or older newly diagnosed with breast cancer or ductal carcinoma in situ between 1992 and 2003, excluding those diagnosed on death certificate or at autopsy (n = 102,184). We then excluded women diagnosed with a second cancer within 12 months after their primary breast cancer diagnosis because health care claims cannot reliably discriminate between procedures performed for the index cancer versus the second cancer (100,404 remaining). We further excluded women who had Medicare-managed care insurance within 2 years before through 1 year after diagnosis because their claims data are incomplete (75,286 remaining), and we further excluded women with gaps in their Medicare coverage (66,951 remaining).

We then considered excluding women missing data on American Joint Committee on Cancer (AJCC) Staging 3rd edition (13.5% overall or 19% of women age 80 to 89 years and 39.5% of women age ≥ 90 years), women with a history of non-breast cancer (8.7%), and women without a histologic diagnosis (3.1%). However, when we considered these three exclusions together, 21.9% of our sample would be excluded, including 48.7% of women age ≥ 90 years (Appendix Table A1, online only). Since our study focused on breast cancer characteristics among the oldest women, we chose not to make these exclusions. Instead, we constructed an algorithm using data available on tumor characteristics (extent, number of positive lymph nodes, lymph node invasion, tumor size, and histology) to impute stage for women with missing stage (Appendix A, online only). After imputing stage, only 1.4% of women were still missing stage data. For cases with both known and imputed (AJCC 3rd edition) stage, we tested the extent to which the two measures agreed beyond chance using a two-sided κ statistic. Because of the observed excellent agreement (the two-sided κ statistic was 0.997), we used imputed stage for those women with missing stage in our primary analyses. Our sample included 49,616 women with known or imputed stage I or II disease.

Tumor Characteristics

From SEER, we obtained data on tumor size, regional lymph node involvement, tumor grade, histology, estrogen receptivity (ER), and progesterone receptivity. Variable definitions can be found in Appendix B (online only).

Treatments

We used data from both SEER and Medicare claims to classify initial treatment with surgery or radiation therapy (RT). We considered women to have received surgical and/or RT if reported in SEER or if there were Medicare claims for these treatments within 12 months following diagnosis. We categorized initial treatment as mastectomy, breast-conserving surgery (BCS) plus RT, BCS alone, or no initial surgery. We used Medicare claims to identify receipt of chemotherapy within 12 months following diagnosis among women with ER-positive and lymph node–positive disease, since this population is thought to derive benefit.[6,7,19] Women were classified as having any claim versus no claim for chemotherapy (Appendix B).

Survival Outcomes

Survival time was measured from the patient's date of diagnosis until death or December 31, 2005, whichever came first. SEER tracks vital status annually, and death certificates are used to capture underlying cause of death (Appendix B).

Covariates

Patient characteristics included race/ethnicity, marital status, SEER registry, metropolitan versus nonmetropolitan residence, and year of diagnosis.[6-8] Because SEER-Medicare data do not provide individual-level data on income and/or education, we used census tract data and substituted ZIP code–level data when census tract data were not available.[20] We grouped median household income and percentage of adults with less than a high school education into quintiles within registry. We defined comorbidity using Klabunde's modification of the Charlson comorbidity index (CCI).[21]

Analyses

We examined sociodemographic and tumor characteristics by age at diagnosis (67 to 69, 70 to 74, 75 to 79, 80 to 84, 85 to 89, and ≥ 90 years), and we examined receipt of treatment by age at diagnosis and stage using the Mantel-Haenszel test of trend. Because of the large sample size, we knew a priori that even small differences in characteristics among age groups would achieve statistical significance; however, we were most interested in trends by age. We additionally examined the proportion of women who were treated with BCS and RT or mastectomy since these treatments are considered standard and equally effective for early-stage breast cancer.[22] Using multinomial logistic regression, we examined the effect of age and comorbidity on receipt of treatments for stage I and II disease separately, adjusting for sociodemographics, tumor characteristics, and year of diagnosis. Since few women did not undergo surgery (n = 843; 1.7%), we did not include "no initial surgery" as a treatment option in these analyses. A category of "missing" was included for each covariate in the models.

To determine the impact of age at diagnosis on breast cancer death, we conducted multivariable Cox proportional hazards regression adjusting for sociodemographic and tumor characteristics, year of diagnosis, initial treatments received, and comorbidity. We censored observations of women alive when follow-up ended. We further tested for interactions between treatment and age at diagnosis on breast cancer mortality. To test for residual confounding, we examined the impact of initial treatment on non-breast cancer survival and overall survival.[23] We present the results for non-breast cancer survival since results were similar. We further examined the impact of chemotherapy on breast cancer survival for the subset of women with ER-negative and lymph node–positive tumors adjusting for all covariates.

We performed sensitivity analyses to examine the robustness of our findings. First, we reassessed the impact of treatment on breast cancer survival with propensity score methods, using the "Greedy" match SAS macro[24] to minimize bias related to the nonrandom assignment of treatment. Next, we limited our sample to women with known AJCC stage, known histology, and those without a history of cancer. All statistical analyses used SAS version 9.1 (SAS Institute, Cary, NC). The institutional review board approved this study.

RESULTS

Sample Characteristics

Of the 49,616 women included in our final study population, 28,897 had stage I and 16,582 had stage II disease. We used imputed stage for 6,571 women (13.2%). Table 1 displays sociodemographic and tumor characteristics by age at diagnosis. Women age ≥ 80 years (21.8%) were more likely than women age 67 to 79 years (15.0%) to have a CCI of 2+.

Table 1. Sample and Tumor Characteristics of Older Women With Stage I and II Breast Cancer

Characteristic	67-69 No.	67-69 %	70-74 No.	70-74 %	75-79 No.	75-79 %	80-84 No.	80-84 %	85-89 No.	85-89 %	≥ 90 No.	≥ 90 %	*P*
No. of patients	7,437		13,774		12,757		8,908		4,707		2,033		
Patient characteristics													
Race/ethnicity													
Non-Hispanic white		85.6		86.3		88.3		90.1		91.3		90.1	< .001
Non-Hispanic black		5.1		5.3		5.1		4.4		4.6		5.1	
Hispanic		3.8		3.5		2.6		2.5		2.0		2.6	
Other		5.6		4.9		4.0		3.0		2.2		2.2	
Marital status													
Currently married		60.3		53.5		42.3		28.7		16.5		7.4	< .001
Not married		37.4		44.4		55.2		68.1		80.1		88.2	
Unknown		2.3		2.3		2.6		3.2		3.5		4.4	
Charlson comorbidity index													
0		67.6		64.3		59.3		56.1		50.9		48.7	< .001
1		17.2		19.3		21.1		21.9		24.4		26.0	
≥ 2		11.2		13.6		17.6		20.1		23.1		24.0	
Unknown		4.0		2.8		2.0		1.9		1.7		1.3	
Year of diagnosis													
1992-1995		38.9		36.6		32.8		33.7		34.2		34.9	< .001
1996-1999		31.9		34.0		33.9		32.5		32.8		32.1	
2000-2003		29.2		29.4		33.3		33.8		33.0		33.0	
Quintiles of median income for area of residence (n = 49,361)													
1st		21.4		21.2		21.6		23.3		25.6		27.9	< .001
2nd		20.1		20.7		21.3		22.3		21.6		21.0	
3rd		19.2		19.5		19.9		19.4		19.6		19.8	
4th		18.7		19.2		19.6		17.8		17.9		16.4	
5th		20.7		19.4		17.7		17.3		15.4		14.9	
Quintiles of education (< 12 years) for those age ≥ 25 in area of residence (n = 49,362)													
1st		20.3		20.6		20.9		20.9		22.1		23.6	< .001
2nd		20.4		19.8		20.4		21.0		21.2		20.7	
3rd		19.5		20.0		19.4		19.5		19.9		20.4	
4th		19.6		19.5		19.8		20.3		19.5		18.5	
5th		20.2		20.1		19.5		18.4		17.3		16.8	
Status of residence													
Metropolitan		91.1		91.7		91.2		90.7		89.6		87.7	< .001
Nonmetropolitan		8.9		8.3		8.8		9.3		10.4		12.3	
Tumor characteristics													
Stage II		34.8		34.0		35.1		37.2		42.3		53.0	< .001
Tumor size, cm													
≤ 1		34.7		34.2		32.4		28.4		21.5		12.5	< .001
1 to ≤ 2		38.5		39.3		39.5		39.1		38.2		35.0	
2 to ≤ 5		22.2		21.8		23.8		27.8		34.4		44.9	
> 5		0.9		0.9		1.1		1.1		1.8		3.2	
Unknown		3.7		3.9		3.3		3.5		4.0		4.5	
Histology													
Ductal		79.1		78.5		77.8		77.8		77.4		72.9	< .001
Lobular		8.0		7.9		8.1		7.1		6.9		5.6	
Mucinous		3.5		4.4		4.7		5.5		5.5		6.5	
Other		8.5		8.4		8.3		8.2		7.9		9.3	
Unknown		0.7		0.9		1.0		1.4		2.3		5.8	
No. of positive lymph nodes													
None examined		11.0		15.3		21.1		34.1		50.1		71.5	< .001
None positive		68.4		64.9		60.5		49.3		35.9		16.8	
1-3/unknown		14.3		13.7		12.7		11.4		9.1		7.2	
4-9		3.9		3.7		3.4		3.3		3.0		2.5	
≥ 10		1.4		1.4		1.4		1.2		0.9		0.9	
Unknown		1.1		1.1		1.0		0.8		1.0		1.1	

Patients in Age Group (years)

(continued on following page)

Table 1. Sample and Tumor Characteristics of Older Women With Stage I and II Breast Cancer (continued)

	Patients in Age Group (years)												
	67-69		70-74		75-79		80-84		85-89		≥ 90		
Characteristic	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	*P*
Among women with examined nodes	6,549		11,542		9,972		5,805		2,313		564		
Positive nodes		22.4		22.5		22.6		24.5		26.9		39.4	< .001
Tumor grade													
1 (Well differentiated)		18.6		21.0		20.9		19.9		18.7		15.5	< .001
2 (Moderately differentiated)		39.4		39.2		40.1		40.3		38.7		37.6	
3 (Poorly differentiated)		26.4		24.4		23.9		24.6		25.4		26.6	
4 (Undifferentiated)		2.0		1.7		1.7		1.6		1.9		1.8	
Unknown		13.6		13.7		13.4		13.6		15.7		18.5	
Among women with known tumor grade	6,429		11,881		11,045		7,693		3,988		1,657		
1 (Well differentiated)		21.6		24.3		24.2		23.0		22.1		19.1	.21
2 (Moderately differentiated)		45.6		45.4		46.3		46.7		45.7		46.2	
3 (Poorly differentiated)		30.6		28.3		27.6		28.5		30.0		32.6	
4 (Undifferentiated)		2.3		2.0		2.0		1.8		2.2		2.2	
Estrogen receptor status													
Positive/borderline		67.3		68.2		70.0		68.2		65.8		61.3	< .001
Negative		15.0		13.7		12.0		11.7		10.6		11.0	
Unknown/not tested		17.8		18.1		18.0		20.1		23.6		27.7	
Among women with known estrogen receptor status	6,116		11,284		10,462		7,122		3,595		1,470		< .001
Positive/borderline		81.8		83.3		85.4		85.4		86.1		84.8	
Negative		18.2		16.7		14.7		14.6		13.9		15.2	
Progesterone receptor status													
Positive/borderline		56.6		57.4		58.4		56.2		53.4		51.1	< .001
Negative		24.0		23.0		22.1		22.4		21.7		19.9	
Unknown/not tested		19.4		19.6		19.5		21.4		25.0		29.0	
Among women with known progesterone receptor status	5,992		11,080		10,272		7,004		3,531		1,445		.05
Positive/borderline		70.2		71.4		72.6		71.5		71.1		71.9	
Negative		29.8		28.7		27.4		28.5		28.9		28.1	
Vital status at end of follow-up period (12/31/2005)													
Alive		74.8		69.1		59.8		45.0		30.2		14.1	< .001
Death due to breast cancer		8.2		7.8		7.8		9.1		11.1		15.3	
Death due to other cause		14.1		19.5		27.5		40.7		53.9		67.4	
Death due to unknown cause		2.9		3.6		4.9		5.3		4.8		3.3	
Among women who died	1,873		4,256		5,130		4,902		3,287		1,747		
Deaths due to breast cancer		32.4		25.3		19.4		16.5		15.9		17.8	< .001

NOTE. Mantel-Haenszel test of trend was used for analyses.

Tumor Characteristics

Among women with known tumor grade and progesterone receptivity status, there were no statistically significant differences by age. Differences in ER positivity by age were small (< 5% differences among those with known receptor status). Tumor size increased with age, and the increase was more dramatic after age 80 years. Similarly, the number of women who did not have lymph nodes examined increased with age, and the rate of increase was more dramatic after age 80. Among women who had their lymph nodes examined, those age ≥ 80 years were disproportionately more likely to have positive nodes detected than women age 67 to 79 years.

Initial Treatments

Nearly all women (98.3%) received some surgery for early-stage breast cancer. For women with stage I disease, treatment with BCS + RT declined with age, particularly after age 80 (Fig 1). Mastectomy was the most common treatment among women age 80 to 84 years. Almost all (91.7%) women age 67 to 79 years with stage I disease received mastectomy or BCS + RT compared with 66.8% of women age ≥ 80 years. Among women with stage II disease, mastectomy was the most common treatment regardless of age (Fig 2). However, BCS + RT declined with age. Nearly all women age 66 to 79 years with stage II disease (94.5%) received BCS + RT or mastectomy compared with 76.1% of women age ≥ 80 years. Among women with ER-negative, lymph node–positive disease, receipt of chemotherapy declined significantly with age (Fig 3).

In multinomial logistic regression, women age ≥ 80 years were significantly more likely than women age 67 to 79 years to be treated with mastectomy (odds ratio [OR], 2.1; 95% CI, 2.0 to 2.2) or with BCS alone (OR, 4.2; 95% CI, 4.0 to 4.6) compared with BCS + RT.

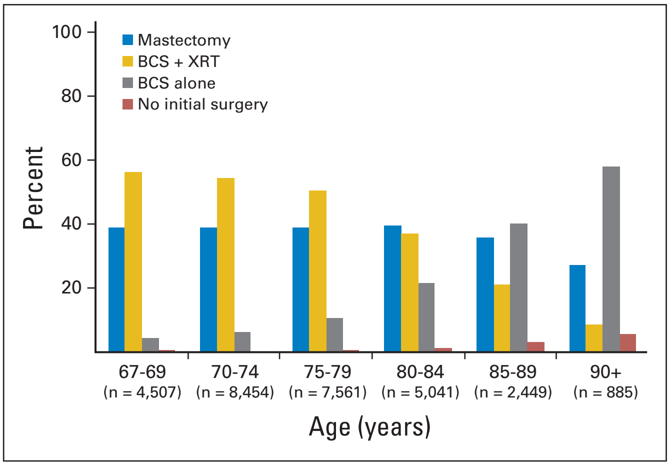

Fig 1. Initial treatment for stage I breast cancer by age at diagnosis. Receipt of treatment differed by age at diagnosis for each stage using the Mantel-Haenszel test of trend ($P < .001$). BCS, breast-conserving surgery; XRT, radiation therapy.

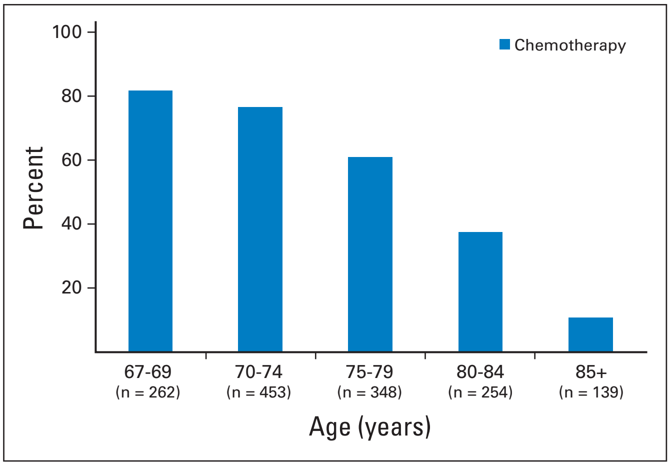

Fig 3. Receipt of chemotherapy among women with estrogen receptor–negative, lymph node–positive, stage I/II breast cancer.

Women with a CCI of 2+ were more likely to receive mastectomy (OR, 1.3; 95% CI, 1.3 to 1.4) or BCS alone (OR, 1.6; 95% CI, 1.5 to 1.8) than BCS + RT. The effect of age was stronger than the effect of comorbidity on receipt of treatment. Among the subset of women with a CCI of 0, 25.8% of women age ≥ 80 years received BCS alone or no surgery compared with 6.0% of women age 65 to 79 years. No significant interactions were observed between age and comorbidity on types of treatment received.

Survival

Overall, median follow-up time was 5.6 years (interquartile range, 3.3 to 8.7). Few women with stage I (4.5%) or stage II (16.1%) disease died of breast cancer. Among women who died, the proportion who died of breast cancer relative to other causes declined with advancing age (Table 1). However, the risk of dying from breast cancer increased significantly with age for women age ≥ 80 years compared with younger women (Table 2). The risk of dying from other causes was greater than the risk of dying from breast cancer at all ages and stages.

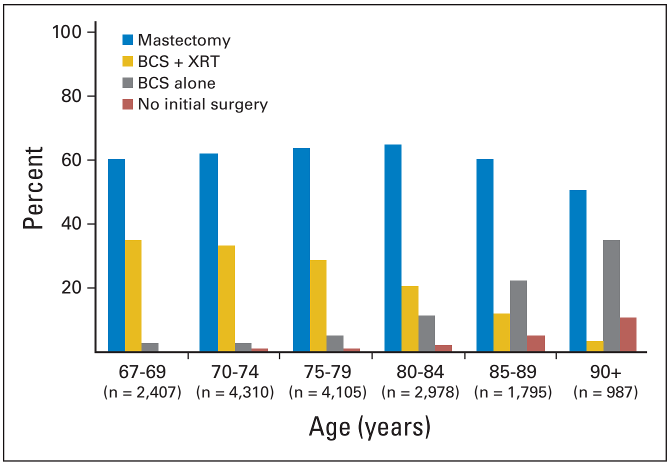

Fig 2. Initial treatment for stage II breast cancer by age at diagnosis. Receipt of treatment differed by age at diagnosis for each stage using the Mantel-Haenszel test of trend ($P < .001$). BCS, breast-conserving surgery; XRT, radiation therapy.

Women treated with mastectomy, BCS alone, or no surgery experienced worse breast cancer survival than those treated with BCS + RT (Appendix Table A1). However, for women treated with either mastectomy or BCS alone, the risk of dying from breast cancer was similar to the risk of dying from other causes. Women who received no surgery had a substantially increased risk of dying from breast cancer compared with those treated with BCS + RT, and this risk exceeded their risk of dying from other causes. However, few women did not receive surgery. No significant interactions were observed between age and treatment on breast cancer mortality; however, interactions between age (67 to 79 *v* ≥ 80 years) and types of treatment were significant for non-breast cancer mortality.

Among women with ER-negative, lymph node–positive breast tumors, we found that chemotherapy reduced breast cancer mortality (adjusted hazard ratio [aHR], 0.8; range, 0.6 to 0.96). Since the interaction of age and chemotherapy was significant ($P = .03$), we performed subgroup analyses. Chemotherapy was associated with a significant reduction in mortality for women age 67 to 79 years (aHR, 0.6; range, 0.5 to 0.8) and an increased risk of mortality for women age ≥ 80 years (aHR, 1.5; range, 0.9 to 2.3) that did not achieve statistical significance. Chemotherapy was associated with improved non-breast cancer survival among all women (aHR, 0.6; range, 0.4 to 0.8).

Sensitivity Analyses

In analyses of women with known AJCC stage, known histologic diagnosis, and no history of cancer, the impact of age, comorbidity, and treatment on survival were similar (data not shown). Overall, our results for the associations between treatment and survival outcomes were also similar using propensity score methods (Table 3).

DISCUSSION

Breast cancer characteristics (eg, tumor grade, histology, hormone receptivity) appear to be similar between women age ≥ 80 years and younger women. However, women age ≥ 80 years receive less aggressive treatment than younger women. Greater comorbidity likely accounts for some of the observed difference; however,

Table 2. HR of Death Due to Breast Cancer and Other Causes by Age at Diagnosis and Stage

	Known AJCC 3rd Edition Stage + Imputed Stage			
Characteristic	HR of Death Due to Breast Cancer	Range	HR of Death Due to Other Causes	Range
Stage I				
Age group, years				
67-69	Reference		Reference	
70-74	1.0	0.9-1.2	1.4	1.3-1.6
75-79	1.1	0.9-1.3	2.2	2.0-2.3
80-84	1.4	1.2-1.7	3.3	3.0-3.5
85-89	1.7	1.3-2.1	4.8	4.3-5.2
≥ 90	2.6	2.0-3.4	7.2	6.5-8.1
Charlson comorbidity index				
0	Reference		Reference	
1	1.2	1.1-1.4	1.7	1.6-1.8
2+	1.7	1.5-1.9	2.7	2.6-2.8
Stage II				
Age group, years				
67-69	Reference		Reference	
70-74	1.0	0.9-1.2	1.3	1.2-1.4
75-79	1.1	0.99-1.3	1.9	1.8-2.2
80-84	1.2	1.1-1.4	3.0	2.7-3.3
85-89	1.5	1.3-1.7	4.1	3.7-4.6
≥ 90	1.8	1.5-2.2	5.9	5.2-6.7
Charlson comorbidity index				
0	Reference		Reference	
1	1.1	1.0-1.3	1.7	1.6-1.8
2+	1.3	1.2-1.4	2.6	2.5-2.8

NOTE. Each model was adjusted for tumor characteristics (grade, hormone receptivity, tumor size, histology, lymph node status [none examined, none positive]; for stage II: one to three positive lymph nodes/unknown number of positive lymph nodes, four or more positive lymph nodes) and sociodemographics (age at diagnosis, marital status, race/ethnicity, educational attainment of census tract/ZIP code, median household income of census tract/income, metropolitan *v* nonmetropolitan status of residence, comorbidities [Charlson comorbidity index], year of diagnosis, tumor registry, and breast cancer treatments).
Abbreviations: HR, hazard ratio; AJCC, American Joint Committee on Cancer.

among women with a Charlson score of 0, 26% of those age ≥ 80 years did not receive standard treatments (mastectomy or BCS + RT) for early-stage breast cancer compared with only 6% of younger women. We also found that the risk of dying from breast cancer increases significantly after age 80. Our findings suggest that we may be able to identify a subgroup of women age ≥ 80 years who may benefit from more aggressive work-up and treatment of their early-stage breast cancer. Conversely, we may also be able to

Table 3. HR for Different Breast Cancer Treatments on Breast Cancer Death and Non-Breast Cancer Death

	Known AJCC Stage + Imputed Stage				Propensity Score Methods (known AJCC stage + imputed stage)			
Characteristic	HR of Death Due to Breast Cancer	Range	HR of Death Due to Other Causes	Range	HR of Death Due to Breast Cancer	Range	HR of Death Due to Other Causes	Range
Stage I								
BCS + RT	Reference		Reference		Reference		Reference	
Mastectomy	1.3	1.2-1.5	1.3	1.2-1.4	1.3	1.1-1.5	1.2	1.2-1.3
BCS alone	1.4	1.2-1.7	1.5	1.4-1.6	1.5	1.2-1.8	1.5	1.4-1.7
No surgery	7.2	5.4-9.6	2.7	2.3-3.2	7.2	3.6-14.3	1.7	1.3-2.3
Stage II								
BCS + RT	Reference		Reference		Reference		Reference	
Mastectomy	1.5	1.3-1.6	1.5	1.4-1.6	1.5	1.3-1.7	1.3	1.2-1.4
BCS alone	1.7	1.5-2.0	1.6	1.4-1.8	1.8	1.4-2.3	1.8	1.5-2.0
No Surgery	5.3	4.2-6.8	2.6	2.2-3.1	3.9	2.2-7.1	2.0	1.4-2.9

NOTE. Each model was adjusted for tumor characteristics (grade, hormone receptivity, tumor size, histology, lymph node status [none examined, none positive]; for stage II: one to three positive lymph nodes/unknown number of positive lymph nodes, four or more positive lymph nodes) and sociodemographics (age at diagnosis, marital status, race/ethnicity, educational attainment of census tract/ZIP code, median household income of census tract/income, metropolitan versus nonmetropolitan status of residence, comorbidities [Charlson comorbidity index], year of diagnosis, tumor registry, and breast cancer treatments).
Abbreviations: HR, hazard ratio; BCS, breast-conserving surgery; RT, radiation therapy.

identify a population of older women on the basis of tumor characteristics, comorbid diseases, and life expectancy who may not need as aggressive treatment. The majority of older women with early-stage disease died from other causes. Future studies are needed to develop tools that can help clinicians appropriately target breast cancer treatments to the oldest women most likely to benefit.

Despite prevailing opinion that breast cancer tumor characteristics are more favorable among older women than younger women, we generally did not find clinically important differences by age at diagnosis for most tumor characteristics. However, the youngest women in our study were older than most women included in other studies.[25] It is possible that tumors present with more favorable characteristics with older age but beyond age 67 years, these differences are negligible. Other studies have also failed to show increases in hormone receptor positivity among women age 70 years and older.[14,26] Although we and others[27] have found that the proportion of women with positive lymph nodes increased with age, we also found that the proportion of women who had their lymph nodes examined declined substantially with age, which may reflect biased sampling. Clinicians may be choosing to sample only lymph nodes of older women who they suspect will be positive.

Regardless of age, we found that the majority of older women undergo surgery for treatment of breast cancer. Among women with stage I disease, BCS + RT is the most common treatment for women age 67 to 79 years. Mastectomy is the most common treatment for women age 80 to 84 years, which may reflect physicians' attempts to treat older women effectively but without radiation. After age 85, BCS alone is the most common treatment. Among women with stage II disease, mastectomy is the most common treatment for all women, regardless of age; however, BCS alone becomes substantially more common after age 80. Some of the oldest women may be undertreated, while others may be being treated appropriately. Future work should focus on identifying tumor and patient characteristics associated with an improved response to aggressive therapy among the oldest women.

As for the impact of RT on older women's breast cancer survival, we found that older women treated with BCS + RT had the best breast cancer survival. However, these women also had the best overall survival, suggesting that unmeasured factors related to survival affected treatment decisions. Clinical trials show that RT after BCS compared with BCS alone reduces breast cancer recurrence among older women with early-stage disease but does not affect survival.[8,28,29] Since we found that breast cancer mortality increases significantly after age 80 and these women are the least likely to be treated aggressively, our findings suggest that some older women in good health may benefit from more aggressive treatment.

We found that treatment with chemotherapy was associated with a survival benefit for women age 67 to 79 years with ER-negative, lymph node–positive disease, results similar to those in other studies.[6,7] However, chemotherapy tended to be associated with worse breast cancer survival among women age ≥ 80 years. Since few women age ≥ 80 years received chemotherapy, our findings suggest that chemotherapy is reserved for the oldest women with the worst tumor characteristics.

This study has several important limitations. Since this is an observational study, there is potential for selection bias and residual confounding by factors for which we do not have data, such as performance status, social support, and treatment with hormonal therapy. In post hoc sensitivity analyses, we examined the effect of an unmeasured confounder such as hormonal therapy on our estimated aHRs. Assuming that treatment with tamoxifen is more common among women age ≥ 80 years than among younger women[30] and that the survival benefit of tamoxifen ranges from 10% to 50% reduction in breast cancer mortality,[31] we found that our aHRs would decrease by less than 10% if we were able to adjust for tamoxifen use.[32,33] Completion of death certificate data could also differ by age. However, studies have found that coding of cancer on death certificates is accurate, particularly coding of breast cancer death.[34,35] In addition, administrative data may underestimate the prevalence of many chronic conditions. Moreover, we needed to exclude women who had missing claims data, the majority of whom had health maintenance organization coverage. Health maintenance organizations tend to include younger and healthier women, which may mean that our sample of women age 67 to 79 years may be older and in poorer health than the overall population. However, this would bias our comparisons between the oldest-old and younger-old toward the null. AJCC staging was modified in 2003 such that women with four or more positive lymph nodes are now classified as stage III. However, only 4.7% of women in our sample had four or more positive nodes. Changes in staging had no effect on women classified as stage I. Finally, although socioeconomic status data were community level, studies have demonstrated moderate associations between individual and aggregate socioeconomic characteristics.[20]

In summary, breast cancer characteristics are similar among women age ≥ 80 years and younger women. However, women age ≥ 80 years receive less aggressive treatment and are more likely to die from breast cancer. Future studies should focus on identifying tumor and patient characteristics that can be used to help target breast cancer treatments to the oldest women most likely to benefit.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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