

Original Investigation

Effect of Breast Conservation Therapy vs Mastectomy on Disease-Specific Survival for Early-Stage Breast Cancer

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IMPORTANCE To our knowledge, there are no recent studies that directly compare survival after breast conservation therapy (BCT) vs mastectomy.

OBJECTIVE To compare the breast cancer–specific survival rates of patients undergoing BCT, mastectomy alone, or mastectomy with radiation using a contemporary cohort of patients.

DESIGN, SETTING, AND PARTICIPANTS We performed univariate, multivariate logistic regression, and propensity analyses to compare the hazard of death for female patients with early-stage invasive ductal carcinoma treated with BCT, mastectomy alone, or mastectomy with radiation during the period from 1998 to 2008. The data were extracted from the Surveillance, Epidemiology, and End Results database. Early-stage breast cancer was defined as having a tumor size of 4 cm or smaller with 3 or less positive lymph nodes.

EXPOSURE Breast conservation therapy, mastectomy alone, or mastectomy with radiation.

MAIN OUTCOMES AND MEASURES Hazard of death due to breast cancer for patients undergoing BCT, mastectomy alone, or mastectomy with radiation.

RESULTS A total of 132 149 patients were included in this analysis. Breast conservation therapy was used to treat 70% of patients, mastectomy alone was used to treat 27% of patients, and mastectomy with radiation was used to treat 3% of patients. The 5-year breast cancer–specific survival rates of patients who underwent BCT, a mastectomy alone, or a mastectomy with radiation were 97%, 94%, and 90%, respectively ($P < .001$); the 10-year breast cancer–specific survival rates were 94%, 90%, and 83%, respectively ($P < .001$). Multivariate analysis showed that women undergoing BCT had a higher survival rate than those undergoing mastectomy alone (hazard ratio, 1.31; $P < .001$) or mastectomy with radiation (hazard ratio, 1.47; $P < .001$). When propensity score stratification was used, the effect of treatment method on survival was similar.

CONCLUSIONS AND RELEVANCE Patients who underwent BCT have a higher breast cancer–specific survival rate compared with those treated with mastectomy alone or mastectomy with radiation for early-stage invasive ductal carcinoma. Further investigation is warranted to understand what may be contributing to this effect.

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Breast conservation therapy (BCT) was recommended as the treatment of choice for women with early-stage breast cancer (stage I or II) by the National Institutes of Health in 1990.¹ Currently, about 60% of patients with early-stage breast cancer undergo BCT.²⁻⁵ These recommendations were based on several randomized controlled trials demonstrating similar survival rates between patients undergoing BCT and those undergoing a mastectomy.⁶⁻¹³ The long-term follow-up in 2 trials (the National Surgical Adjuvant Breast and Bowel Project B-06⁷ and the Milan trial¹³) confirmed that there was no difference in survival rates after 20 years. Over the 40 years since these trials were conducted, substantial changes in breast cancer detection and treatment have occurred, including a new understanding of tumor biology and advances in adjuvant therapy.

To our knowledge, there are no recent randomized trials comparing BCT (lumpectomy followed by radiation) with mastectomy alone (without postmastectomy radiation). Meanwhile, several robust data sets exist that allow for a contemporary comparison of patients undergoing BCT and patients undergoing a mastectomy. In the present study, we use patient-level data from the Surveillance, Epidemiology, and End Results (SEER) database to compare the survival rates of patients with early-stage breast cancer who underwent BCT, a mastectomy alone, or a mastectomy with radiation during the period from 1998 to 2008.

Methods

Data Source

Population-level de-identified data were extracted from the SEER cancer database (November 2012 submission) with follow-up until 2010. The SEER database is a national effort that collects patient-level data for all index malignant tumors in 18 cancer registries across the United States and captures 28% of the nation's population.¹⁴ This database is regarded as nationally representative and contains detailed demographic, socioeconomic, cancer, and treatment information. To ensure data accuracy, chart abstracters undergo extensive training. Malignant tumors are encoded by use of the ninth revision of the *International Classification of Diseases for Oncology*.

This study did not meet the University of Utah's criteria for requiring institutional review board approval or exemption because it involved the use of a national dataset of de-identified patient information and did not meet the definitions of human subjects research according to federal regulations. Patient consent was not obtained because the SEER database contains retrospective data that are de-identified.

Inclusion and Exclusion Criteria

Data were extracted from the SEER database for all female patients with a unilateral, invasive ductal breast cancer (*International Classification of Diseases for Oncology* code 8500) who underwent unilateral lumpectomy (site-specific surgery codes 20-24) with radiation, mastectomy alone (site-specific surgery codes 41 and 51), or mastectomy with postsurgical radiation during the period from 1998 to 2008. All other breast can-

cer histologies were excluded. All patients who underwent bilateral treatment for unilateral breast cancer were excluded. Only patients with new primary breast cancers were included. Only those patients with a tumor size of 4 cm or smaller and 3 or less positive lymph nodes were included. Patients with 4 or more positive lymph nodes were excluded because these patients would likely be indicated to receive radiation regardless of having undergone a mastectomy or lumpectomy.

Statistical Analysis

The demographic characteristics accounted for in our analysis included the year of diagnosis (continuous variable), age, and race. Age was limited to 18 to 80 years and was divided into categories (≤ 35 , 36-50, 51-65, and > 65 years). Race/ethnicity was coded as white, black, other, and unknown. The oncologic characteristics in our analysis included the number of positive lymph nodes (0 or 1-3), tumor size (≤ 2 cm vs > 2 to 4 cm), estrogen receptor and progesterone receptor status, and tumor grade.

Treatment groups were assessed for imbalance across demographic and oncologic data. Significant associations were determined using Pearson tests for categorical associations and Kruskal-Wallis tests for continuous associations. Survival was analyzed with univariate and multivariate statistical methods. Nonparametric survival analysis using the Kaplan-Meier method was performed to estimate 5- and 10-year survival and to investigate the survival effects of treatment group within tumor size groups and lymph node status. Log-rank tests were used to determine differences between these survival curves. Unadjusted Cox proportional hazards models were used to assess the effects of treatment groups, as well as demographic and oncologic factors, on cause-specific survival. A multivariate Cox proportional hazards regression model was used to evaluate the effect of treatment method (BCT, mastectomy alone, or mastectomy with radiation) on survival while controlling for the demographic and oncologic factors already mentioned. The assumptions of the Cox model were examined, and because estrogen receptor status and age failed to meet the assumption of proportionality, stratification was used to include the effect of these variables.

Separately, propensity analysis was used to compare treatment groups within sets of patients with a similar likelihood for a given treatment. Propensity scores were determined by fitting a multivariate logistic regression model adjusted for year of diagnosis, age at diagnosis, race, tumor grade, estrogen receptor and progesterone receptor status, tumor size, and node status. Two separate models were used to generate propensity scores to determine the likelihood that a given patient would undergo (1) BCT or (2) mastectomy with no radiation. Using the final Cox model, we then estimated the effect of the 3 treatment groups, allowing the baseline survival function to vary by including quartiles of these propensity scores as stratification variables. Beyond the inclusion exclusion criteria, there were no missing data because categories for "unknown" were included in the analysis.

All statistical analyses were performed with SAS version 9.3 (SAS Institute Inc) and R version 2.15 (R Development Core

Table 1. Population Descriptive Statistics

| Characteristic | Patients, No. (%) | | | Test Statistic | P Value |
|------------------------------------|--|-------------------------------|--|---------------------------|--------------------|
| | Breast Conservation Therapy (n = 92 671) | Mastectomy Alone (n = 34 999) | Mastectomy With Radiation (n = 44 799) | | |
| Median age at diagnosis (range), y | 57 (49-66) | 61 (50-70) | 52 (44-62) | $F_{2, 132, 146} = 871.8$ | <.001 ^a |
| Median year of diagnosis | 2004 | 2003 | 2003 | $F_{2, 132, 146} = 157.2$ | <.001 ^a |
| Race | | | | | |
| White | 77 881 (84) | 27 335 (78) | 3357 (75) | $\chi^2_4 = 909.9$ | <.001 ^b |
| Black | 7426 (8) | 3279 (9) | 577 (13) | | |
| Other | 7364 (8) | 4385 (13) | 545 (12) | | |
| Tumor grade | | | | | |
| I | 21 597 (23) | 5599 (16) | 395 (9) | $\chi^2_8 = 1991$ | <.001 ^b |
| II | 39 186 (42) | 14 246 (41) | 1643 (37) | | |
| III | 28 982 (31) | 13 444 (38) | 2232 (50) | | |
| IV | 966 (1) | 572 (2) | 92 (2) | | |
| Unknown | 1940 (2) | 1138 (3) | 117 (3) | | |
| ER status | | | | | |
| Negative | 17 309 (19) | 7911 (23) | 1252 (28) | $\chi^2_4 = 1833$ | <.001 ^b |
| Positive | 69 887 (75) | 23 006 (66) | 2902 (65) | | |
| Unknown | 5475 (6) | 4082 (12) | 325 (7) | | |
| PR status | | | | | |
| Negative | 25 645 (28) | 11 147 (32) | 1640 (37) | $\chi^2_4 = 1755$ | <.001 ^b |
| Positive | 60 115 (65) | 19 105 (55) | 2450 (55) | | |
| Unknown | 6911 (7) | 4747 (14) | 389 (9) | | |
| Size, cm | | | | | |
| ≤2 | 74 439 (80) | 22 568 (64) | 2043 (46) | $\chi^2_2 = 5523$ | <.001 ^b |
| >2 to 4 | 18 232 (20) | 12 431 (36) | 2436 (54) | | |
| Lymph nodes | | | | | |
| Positive (1-3 nodes) | 18 514 (20) | 10 333 (30) | 2861 (64) | $\chi^2_2 = 5313$ | <.001 ^b |
| Negative | 74 157 (80) | 24 666 (70) | 1618 (36) | | |

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

^a Determined by use of the Kruskal-Wallis test.

^b Determined by use of the Pearson test.

Team for the R Foundation for Statistical Computing). Tests were deemed statistically significant at the α level of .05.

Results

Description of Population

A total of 132 149 patients were included in this analysis. Breast conservation therapy was used for the treatment of 92 671 patients (70.1%), mastectomy alone for the treatment of 34 999 patients (26.5%), and mastectomy with radiation for the treatment of 44 799 patients (3.4%). The median ages of women undergoing BCT, mastectomy alone, or mastectomy with radiation were 57, 61, and 52 years, respectively. A higher percentage of patients who underwent a mastectomy alone or who underwent a mastectomy with radiation had a larger tumor size (>2 to 4 cm) than did patients who received BCT. A higher percentage of patients who underwent a mastectomy alone or who underwent a mastectomy with radiation also had positive lymph nodes compared with patients who received BCT (Table 1). Analysis of treatment type by year demonstrated minimal differences in the annual use of BCT, mastectomy alone, or mastectomy with radiation (Table 2).

Breast Cancer-Specific Survival and Kaplan-Meier Analysis

The 5-year breast cancer-specific survival rates for patients who underwent BCT, a mastectomy alone, or a mastectomy with radiation were 97% (95% CI, 97%-97%), 94% (95% CI, 94%-94%), and 90% (95% CI, 89%-91%), respectively. The 10-year breast cancer-specific survival rates for patients treated with BCT, mastectomy alone, or mastectomy with radiation were 94% (95% CI, 94%-94%), 90% (95% CI, 89%-90%), and 83% (95% CI, 82%-85%), respectively. Log-rank tests indicated significantly different survival curves at the 5- and 10-year points ($P < .001$) (Figure 1). Kaplan-Meier survival analysis of patients stratified by treatment method and tumor size demonstrated higher survival for patients who received BCT compared with their tumor size-matched cohorts treated with mastectomy alone or mastectomy with radiation (Figure 2). Kaplan-Meier survival analysis of patients stratified by treatment method and lymph node status demonstrated higher survival for patients who received BCT compared with their lymph node-matched cohorts treated with mastectomy alone or mastectomy with radiation (Figure 3). Even when controlling for lymph node status, we found that when patients were stratified based on a tumor size of 2 cm or smaller or a tumor size of larger than 2

Table 2. Frequency of Surgery Type by Year

| Year of Diagnosis | Type of Surgery, No. (%) of Patients | | | Total |
|-------------------|--------------------------------------|------------------|---------------------------|---------|
| | Breast Conservation Therapy | Mastectomy Alone | Mastectomy With Radiation | |
| 1998 | 4154 (67.3) | 1820 (29.5) | 198 (3.2) | 6172 |
| 1999 | 4314 (67.6) | 1810 (28.4) | 255 (4.0) | 6379 |
| 2000 | 8438 (68.3) | 3429 (27.7) | 497 (4.0) | 12 364 |
| 2001 | 8452 (66.4) | 3826 (30.0) | 456 (3.6) | 12 734 |
| 2002 | 8520 (67.5) | 3706 (29.3) | 400 (3.2) | 12 626 |
| 2003 | 8940 (69.7) | 3434 (26.8) | 448 (3.5) | 12 822 |
| 2004 | 9301 (70.2) | 3528 (26.6) | 417 (3.2) | 13 246 |
| 2005 | 9618 (72.5) | 3237 (24.4) | 416 (3.1) | 13 271 |
| 2006 | 9855 (72.7) | 3315 (24.5) | 384 (2.8) | 13 554 |
| 2007 | 10 467 (72.4) | 3458 (23.9) | 528 (3.7) | 14 453 |
| 2008 | 10 612 (73.1) | 3436 (23.6) | 480 (3.3) | 14 528 |
| Total | 92 671 | 34 999 | 4479 | 132 149 |

Figure 1. Kaplan-Meier Survival Analysis Stratified by Treatment Type

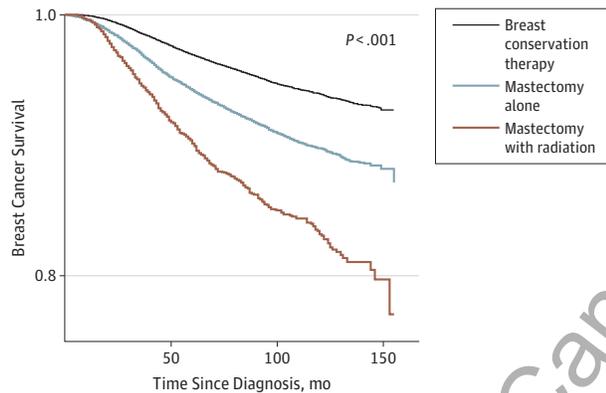


Figure 3. Kaplan-Meier Survival Analysis Stratified by Treatment Type and Lymph Node Status

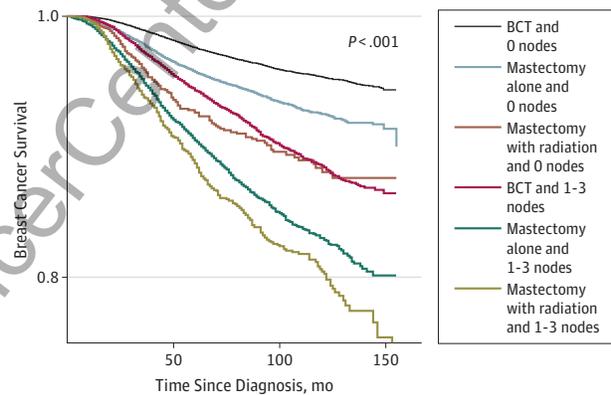
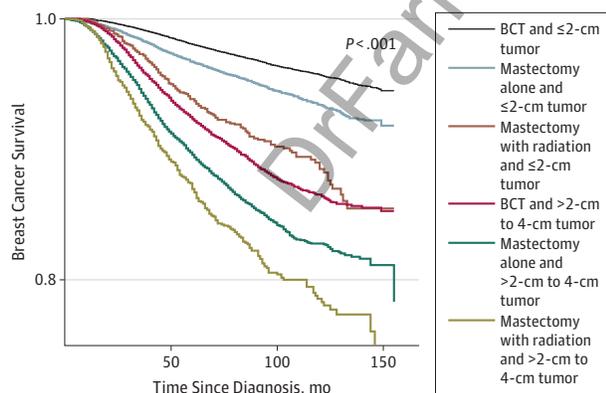


Figure 2. Kaplan-Meier Survival Analysis Stratified by Treatment Type and Tumor Size



BCT indicates breast conservation therapy.

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to 4 cm, those who received BCT continued to exhibit improved survival when compared with patients treated with mastectomy alone or mastectomy with radiation (Figure 4A and B).

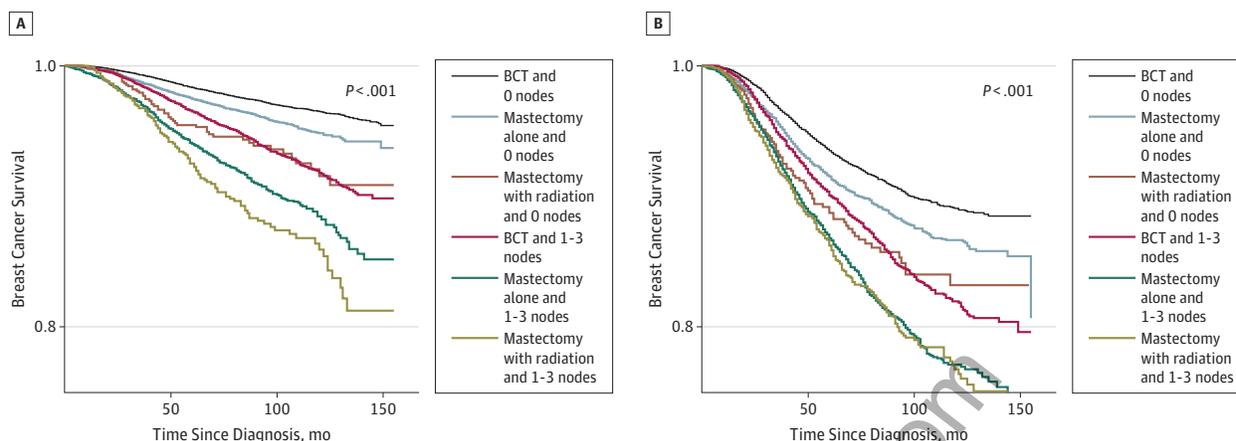
Univariate Analysis of Breast Cancer-Specific Survival

Univariate analysis indicated that patients who received a mastectomy alone (hazard ratio [HR], 1.82 [95% CI, 1.73-1.91]) or a mastectomy with radiation (HR, 3.17 [95% CI, 2.89-3.47]) were more likely to die of their disease compared with patients receiving BCT. Age at diagnosis was not associated with significant differences in breast cancer-specific survival. Being black was associated with a higher hazard of death (HR, 1.93 [95% CI, 1.81-2.07]) compared with being white. A larger tumor size (>2 to 4 cm) was associated with higher odds of death (HR, 3.61 [95% CI, 3.44-3.79]) compared with a tumor size of 2 cm or smaller; negative lymph node status was associated with decreased odds of death (HR, 0.38 [95% CI, 0.36-0.40]) (Table 3).

Multivariate Analysis of Breast Cancer-Specific Survival

Women undergoing a mastectomy alone had a higher hazard of death (HR, 1.31 [95% CI, 1.25-1.39]) than those undergoing BCT. Women undergoing a mastectomy with radiation also had a higher hazard of death (HR, 1.47 [95% CI, 1.34-1.61]) than those

Figure 4. Kaplan-Meier Survival Analysis Stratified by Tumor Size, Treatment Type, and Lymph Node Status



Some patients had a tumor size of 2 cm or smaller (A), whereas others had a tumor size in the range of larger than 2 to 4 cm (B). BCT indicates breast conservation therapy.

undergoing BCT. Race was an independent predictor of increased hazard of death; black patients continue to have a higher hazard of death (HR, 1.35 [95% CI, 1.26-1.45]) than white patients, despite controlling for other demographic and tumor characteristics. Women with larger tumors (>2 to 4 cm) had a greater hazard of death (HR, 2.11 [95% CI, 2.00-2.22]) than did patients with a tumor size of 2 cm or smaller. Finally, patients with node-negative tumors had a lower hazard of death (HR, 0.51 [95% CI, 0.48-0.53]) than those who had 1 to 3 positive nodes (Table 4).

Propensity Score Analysis of Breast Cancer-Specific Survival

Propensity scores were used to create strata in which the likelihood of having a given treatment was similar, regardless of the treatment actually received. The Cox proportional hazards model, stratified by propensity score quartile, supported the findings from the multivariate model described—women undergoing a mastectomy alone had a significantly higher hazard of death (HR, 1.32 [95% CI, 1.25-1.39]) than those undergoing BCT. Similar to our multivariate model, women who underwent a mastectomy with radiation had a significantly higher hazard of death (HR, 1.90 [95% CI, 1.73-2.08]) than those who underwent BCT.

Conclusions

Our Findings

For our study, we used the SEER database, which stores cancer data on incidence, treatment, and survival from multiple regions across the nation.¹⁴ More than 130 000 patients are included in our study, of whom 70.1% underwent BCT, 26.5% underwent a mastectomy alone, and 3.4% underwent a mastectomy and radiation. Kaplan-Meier survival analysis demonstrates significantly improved 5- and 10-year breast cancer-specific survival rates in the BCT cohort compared with the mastectomy alone or mastectomy with radiation cohorts; this was confirmed by our multivariate analysis. Multivariate

analysis also demonstrates decreased survival rates associated with black patients, lymph node-positive patients, and patients with a larger tumor size (>2 to 4 cm). Estimates from the multivariate model are not greatly different from the propensity score analysis for patients who received BCT or underwent a mastectomy alone, indicating that the estimate effect is not biased by model selection for these treatment methods. The fact that our model identifies poor survival associated with lymph node involvement and larger tumor size is not surprising, and it may serve as validation of our model.

Survival After BCT vs Mastectomy Alone

Kaplan-Meier analysis of our study population demonstrates that, among patients with a tumor size of 2 cm or smaller or of larger than 2 to 4 cm, those undergoing BCT had a higher survival rate than those undergoing a mastectomy alone. Crowe et al¹⁵ have also previously demonstrated a similar correlation between tumor size and survival. Our analysis also shows that patients who received BCT have a higher breast cancer-specific survival rate than node-matched patients undergoing a mastectomy alone. Gobardhan et al¹⁶ have similarly demonstrated that, among patients with early-stage breast cancer, involvement of 1 to 3 lymph nodes is associated with worse overall survival.

Our findings are similar to those of Hwang et al,¹⁷ who showed a lower hazard of death associated with BCT. In their analysis,¹⁷ only patients from California who received a diagnosis of stage I or II breast cancer during the period from 1990 to 2004 were included. They concluded that the presence of unaccounted variables representing tumor aggressiveness (eg, lymphovascular invasion or extranodal extension) were unlikely to have contributed to such a significant survival difference between the BCT and mastectomy groups. Further studies would be required to verify this claim. Our study further supports the findings of Hwang et al¹⁷ and benefits from the inclusion of multiple regions across the United States and a more contemporary patient population.

Table 3. Univariate Analysis of Survival With Regard to All Patients

| Characteristic | Hazard Ratio (95% CI) | P Value |
|-----------------------------|-----------------------|---------|
| Treatment | | |
| Breast conservation therapy | 1.00 [Reference] | |
| Mastectomy alone | 1.82 (1.73-1.91) | <.001 |
| Mastectomy with radiation | 3.19 (2.89-3.47) | <.001 |
| Diagnosis year | 0.95 (0.94-0.96) | <.001 |
| Age | 0.99 (0.99-1.00) | <.001 |
| Race | | |
| White | 1.00 [Reference] | |
| Black | 1.93 (1.81-2.07) | <.001 |
| Other | 0.84 (0.77-0.93) | <.001 |
| Tumor grade | | |
| I | 1.00 [Reference] | |
| II | 3.49 (3.07-3.96) | <.001 |
| III | 9.60 (8.50-10.86) | <.001 |
| IV | 8.83 (7.26-10.75) | <.001 |
| Unknown | 4.01 (3.27-4.91) | <.001 |
| ER status | | |
| Negative | 1.00 [Reference] | |
| Positive | 0.30 (0.29-0.32) | <.001 |
| Unknown | 0.51 (0.47-0.55) | <.001 |
| PR status | | |
| Negative | 1.00 [Reference] | |
| Positive | 0.33 (0.31-0.35) | <.001 |
| Unknown | 0.59 (0.55-0.64) | <.001 |
| Size, cm | | |
| ≤2 | 1.00 [Reference] | |
| >2 to 4 | 3.61 (3.44-3.79) | <.001 |
| Lymph nodes | | |
| Positive (1-3 nodes) | 1.00 [Reference] | |
| Negative | 0.38 (0.36-0.40) | <.001 |

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

The improved survival noted among patients who received BCT may be due to differences related to adjuvant therapy, such as chemotherapy administration or radiation delivery. In our analysis, we are unable to account for chemotherapy because this variable is not consistently recorded in the SEER database. Furthermore, because the National Comprehensive Cancer Network guidelines do not differentiate between BCT and mastectomy when determining adjuvant systemic therapy, these guidelines should not bias outcomes when comparing BCT with mastectomy. However, we acknowledge that it is possible that systemic therapies are used differently for patients who received BCT vs those who underwent a mastectomy—if this is true, it deserves further assessment. Data from the MA.20 trial¹⁸ suggest that regional nodal radiation, in addition to whole-breast radiation, for lymph node-positive patients may offer a survival advantage when compared with patients who do not receive regional nodal radiation. Finally, other factors such as differences in tumor biology (eg, lymphovascular invasion or extranodal invasion) may contribute to the survival difference, although, as Hwang et al¹⁷ have suggested, we would not expect this factor to have such a large impact.

Table 4. Multivariate Analysis of Survival With Regard to All Patients

| Characteristic | Hazard Ratio (95% CI) | P Value |
|-----------------------------|-----------------------|---------|
| Treatment method | | |
| Breast conservation therapy | 1.00 [Reference] | |
| Mastectomy alone | 1.31 (1.25-1.39) | <.001 |
| Mastectomy with radiation | 1.47 (1.34-1.61) | <.001 |
| Year of diagnosis | 0.95 (0.94-0.96) | <.001 |
| Race | | |
| White | 1.00 [Reference] | |
| Black | 1.35 (1.26-1.45) | <.001 |
| Other | 0.78 (0.71-0.86) | <.001 |
| Tumor grade | | |
| I | 1.00 [Reference] | |
| III | 4.61 (4.06-5.24) | <.001 |
| IV | 4.17 (3.41-5.09) | <.001 |
| Unknown | 2.70 (2.20-3.32) | <.001 |
| PR status | | |
| Negative | 1.00 [Reference] | |
| Positive | 0.66 (0.61-0.71) | <.001 |
| Unknown | 0.86 (0.72-1.02) | .08 |
| Tumor size, cm | | |
| ≤2 | 1.00 [Reference] | |
| >2 to 4 | 2.11 (2.00-2.22) | <.001 |
| Lymph nodes | | |
| Positive (1-3 nodes) | 1.00 [Reference] | |
| Negative | 0.51 (0.48-0.53) | <.001 |

Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

Survival After Mastectomy With Radiation

We performed a survival analysis of patients treated with mastectomy and radiation to further investigate whether radiation may confer a survival advantage to patients. However, our regression analysis demonstrates that patients who undergo a mastectomy with radiation have worse survival rates than patients who undergo BCT. We would have expected that stage-matched patients with similar tumors undergoing a mastectomy with radiation would have a similar survival rate as patients receiving lumpectomy with radiation (ie, BCT). We note that the patients who underwent a mastectomy with radiation tended to be younger, to have high-grade tumors (which were larger in size), and were more likely to be node-positive compared with patients who underwent BCT or a mastectomy alone. Because these factors are accounted for in our multivariate model, these findings suggest that patients who underwent a mastectomy with radiation had a different, perhaps more aggressive, tumor biology not accounted for by our model. It is possible that the decision to perform postmastectomy radiation was related to tumor characteristics such as lymphovascular invasion, extranodal invasion, or size of nodal metastases, all of which portend a poorer prognosis. We find it unlikely that patients who had a mastectomy with radiation are at a survival disadvantage compared with patients who received BCT and who meet National Comprehensive Cancer Network criteria for BCT, thereby suggesting that patients undergoing a mastectomy with radiation are implicitly different from those undergoing BCT.

Prior Clinical Trials

The National Surgical Adjuvant Breast and Bowel Project B-06 compared lumpectomy with or without radiation vs mastectomy in the treatment of stage I or II breast cancer. A total of 1843 patients were included in the final analysis, with a roughly even number of patients in each treatment arm. At 5 years, Fisher et al^{7,8} reported an 82% overall survival rate in the total mastectomy group and a 92% overall survival rate in the lumpectomy with radiation group, but they failed to show statistical significance ($P = .09$). The Milan trial¹³ enrolled 701 patients during the period from 1970 to 1983 who had tumor sizes of less than 2 cm in diameter and no palpable lymph nodes to undergo either a radical mastectomy or a quadrantectomy, an axillary dissection, and radiotherapy. Veronesi et al¹³ reported an overall 5-year survival rate of 90% in both groups and improved disease-free survival rates for patients receiving a quadrantectomy, an axillary dissection, and radiotherapy. In addition, the US National Cancer Institute failed to show a statistically significant difference in survival rates between patients with stage I or II breast cancer who underwent a mastectomy and patients with stage I or II breast cancer who underwent BCT; Lichter et al¹⁰ showed a 5-year survival rate of 85% for mastectomy-treated patients and of 89% for patients who received BCT ($P = .49$), with a total of 247 patients.

Key Differences

Our study evaluates patients treated between 1998 and 2008; this represents a significant difference in the time frame when compared with previous clinical trials.^{6-11,13} Although the present study is limited by our use of a database, it benefits from the large number of patients with a broad range demographic characteristics—nearly 30 times the number of patients enrolled in all 6 clinical trials combined and more than 60 times more patients than in the largest trial (ie, the National Surgical Adjuvant Breast and Bowel Project).⁷⁻⁹ Finally, our study analyzes data from multiple institutions in multiple regions across the United States, and it is representative of the national experience with BCT and mastectomy alone in the treatment of early-stage breast cancers.

Limitations

Our study is subject to the usual limitations of database analyses. We are limited by the quality of data reporting and collection in the SEER database; however, the chart abstractors are rigorously trained to collect and report data accurately. In ad-

dition, our study is a retrospective analysis of prospectively collected data, thus differing from previous prospective randomized controlled trials. As a result, patients in our study were selected to undergo BCT, a mastectomy alone, or a mastectomy with radiation based on a variety of factors, some of which may not be accounted for by our study or reported in the SEER database. For example, SEER does not report patient comorbidities that may present an inherent selection bias in the decision to perform BCT vs mastectomy. It should be noted that our study specifically assesses breast cancer-specific survival and therefore does not include deaths attributable to other causes.

Our study is also limited by lack of tumor biology information such as lymphovascular invasion, extracapsular invasion, and size of nodal metastases, which are not reliably reported by the SEER database, and may portend a poorer prognosis. The SEER database also does not report systemic adjuvant therapy such as chemotherapy, endocrine therapy, or Herceptin use. We would expect that patients with a tumor size greater than 2 cm or with positive lymph nodes may have indications for systemic chemotherapy. This would be true for patients in the mastectomy or BCT groups, thereby minimizing a disproportionate impact of this variable. Use of endocrine therapy or Herceptin is indicated based on the receptor status of tumors, not on the method of surgical treatment that patients receive. The SEER database also does not provide detailed information regarding the field of radiation that patients receive. Finally, although our study assesses breast cancer-specific survival, it cannot account for recurrence rates or disease-free survival. Therefore, we are unable to determine whether patients treated in one group were more likely than patients in the other groups to experience recurrence and require further treatment.

Conclusions

Our analysis of a large and contemporary cohort of patients demonstrates that patients who undergo BCT have improved breast cancer-specific survival compared with patients who undergo mastectomy alone or mastectomy with radiation for early-stage invasive ductal carcinoma. The finding of improved survival with BCT in this large database study could be due to differences in adjuvant therapy regimens or tumor biology. These findings deserve further investigation to determine which factors may be contributing to this effect.

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