**Research Article**

**Survival Outcomes of Breast-Conserving Therapy versus Mastectomy in Early-Stage Breast Cancer, Including Centrally Located Breast Cancer: A SEER-Based Study**

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Received 12 May 2022; Accepted 29 July 2022; Published 27 August 2022

Academic Editor: Junwon Min

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**Purpose.** This study aims to analyze the survival outcomes of breast cancer (BC) patients, especially centrally located breast cancer (CLBC) patients undergoing breast-conserving therapy (BCT) or mastectomy. Methods. Surveillance, epidemiology, and end results (SEER) data of patients with T1-T2 invasive ductal or lobular breast cancer receiving BCT or mastectomy were reviewed. We used X-tile software to convert continuous variables to categorical variables. Chi-square tests were utilized to compare baseline information. The multivariate logistic regression model was performed to evaluate the relationship between predictive variables and treatment choice. Survival outcomes were visualized by Kaplan–Meier curves and cumulative incidence function curves and compared using multivariate analyses, including the Cox proportional hazards model and competing risks model. Propensity score matching was performed to alleviate the effects of baseline differences on survival outcomes. Result. A total of 180,495 patients were enrolled in this study. The breast preservation rates fluctuated around 60% from 2000 to 2015. Clinical features including invasive ductal carcinoma (IDC), lower histologic grade, smaller tumor size, fewer lymph node metastases, positive ER and PR status, and chemotherapy use were independently correlated with BCT in both BC and CLBC cohorts. In all the classic Cox models and competing risks models, BCT was an independent favorable prognostic factor for BC, including CLBC patients in most subgroups. In addition, despite the low breast-conserving rate compared with tumors located in other areas, CLBC did not impair the prognosis of BCT patients. Conclusion. BCT is optional and preferable for most early-stage BC, including CLBC patients.

1. **Introduction**

Breast-conserving therapy (BCT), which refers to breast-conserving surgery plus postoperative radiotherapy, is considered a standard treatment for early-stage breast cancer. Several clinical trials, including NSABP B-06, Milan, and EORTC 10801, have proven that the survival outcomes of patients treated with BCT are equivalent to those undergoing mastectomy, despite a relatively higher risk of local recurrence [1–3]. In addition, BCT patients have significantly improved body image, satisfaction with treatment and sexual functioning, and there was no significant difference in fear of recurrence between patients treated with BCT and mastectomy [4, 5].

Centrally located breast cancer (CLBC) usually refers to tumors located in the area within 2 cm of the nipple-areola complex (NAC) but without NAC involvement. Because of the particularity of its position, surgeons are often not inclined to perform BCT in CLBC. To date, there are only limited studies focused on the safety and prognosis of BCT compared with mastectomy in CLBC, and none of these studies are comprehensive enough [6–8].

To this end, we conducted a detailed retrospective study based on the SEER database to evaluate the prognosis of BC
patients undergoing BCT and mastectomy, especially CLBC patients. Moreover, we used both the classic Cox proportional hazards model and competing risks model to ensure the rigor of this research and reduce statistical errors. Furthermore, we performed a series of subgroup analyses to help surgeons make the best choice according to the patient’s baseline information.

2. Materials and Methods

2.1. Participants. The data for this study were extracted from research plus data from 18 registries of the SEER database released in November 2020. We enrolled 180,495 female patients who received mastectomy or BCT (breast-conserving surgery plus postoperative radiotherapy) after Surveillance, Epidemiology, and End Results (SEER) database released in November 2020.

Table 1: Comparison of baseline characteristics between BC patients undergoing BCT and mastectomy from 2000 to 2015.

| Characteristics | Mastectomy | BCT | p-value |
|-----------------|------------|-----|---------|
| **N** | **%** | **N** | **%** |
| **Year** | | | | < 0.001 |
| 2000–2003 | 11629 | 18.8% | 21347 | 18.0% |
| 2004–2007 | 13304 | 21.5% | 26570 | 22.4% |
| 2008–2015 | 37010 | 59.7% | 70635 | 59.6% |
| **Age, years** | | | < 0.001 |
| 18–63 | 43013 | 69.4% | 77456 | 65.3% |
| 64–72 | 11678 | 18.9% | 28108 | 23.7% |
| 73–79 | 7252 | 11.7% | 12988 | 11.0% |
| **Race** | | | < 0.001 |
| White | 48880 | 78.9% | 97410 | 82.2% |
| Black | 6167 | 10.0% | 11112 | 9.4% |
| Others | 6896 | 11.1% | 10030 | 8.5% |
| **Histologic type** | | | < 0.001 |
| IDC | 56391 | 91.0% | 110183 | 92.9% |
| ILC | 5552 | 9.0% | 8369 | 7.1% |
| **Laterality** | | | 0.698 |
| Left | 31577 | 51.0% | 60549 | 51.1% |
| Right | 30366 | 49.0% | 58003 | 48.9% |
| **Grade** | | | < 0.001 |
| I | 10720 | 17.3% | 30405 | 25.6% |
| II | 26520 | 42.8% | 51602 | 43.5% |
| III/IV | 24703 | 39.9% | 36545 | 31.0% |
| **T stage** | | | < 0.001 |
| T1a | 4283 | 6.9% | 9494 | 8.0% |
| T1b | 9083 | 14.7% | 28637 | 24.2% |
| T1c | 23164 | 37.4% | 52213 | 44.0% |
| T2 | 25413 | 41.0% | 28208 | 23.8% |
| **N stage** | | | < 0.001 |
| N0 | 42422 | 68.5% | 92001 | 77.6% |
| N1 | 15855 | 25.6% | 21863 | 18.4% |
| N2 | 2530 | 4.1% | 3417 | 2.9% |
| N3 | 1136 | 1.8% | 1271 | 1.1% |
| **ER** | | | < 0.001 |
| Negative | 14117 | 22.8% | 19820 | 16.7% |
| Positive | 47826 | 77.2% | 98732 | 83.3% |
| **PR** | | | < 0.001 |
| Negative | 20801 | 33.6% | 31423 | 26.5% |
| Positive | 41142 | 66.4% | 87129 | 73.5% |
| **Chemotherapy** | | | < 0.001 |
| No or unknown | 33049 | 53.4% | 68605 | 57.9% |
| Yes | 28894 | 46.6% | 49947 | 42.1% |

BCT, breast-conserving therapy; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ER, estrogen receptor; PR, progesterone receptor.

Figure 1: The proportion of BC patients undergoing BCT or mastectomy from 2000 to 2015. BCT, breast-conserving therapy.

Table 2: Multivariate logistic regression analysis of factors associated with BCT.

| Characteristics | OR | 95% CI | p-value |
|-----------------|----|--------|---------|
| **Year** | | | < 0.001 |
| 2000–2003 vs. 2008–2015 | 0.994 | 0.967–1.020 | 0.634 |
| 2004–2007 vs. 2008–2015 | 1.082 | 1.055–1.110 | < 0.001 |
| **Age, years** | | | < 0.001 |
| 64–72 vs. 18–63 | 1.306 | 1.273–1.340 | < 0.001 |
| 73–79 vs. 18–63 | 1.028 | 0.994–1.062 | 0.105 |
| **Race** | | | < 0.001 |
| Black vs. white | 1.054 | 1.019–1.091 | 0.003 |
| Others vs. white | 0.747 | 0.722–0.772 | < 0.001 |
| **Histological type** | | | < 0.001 |
| IDC vs. ILC | 1.367 | 1.317–1.418 | < 0.001 |
| **Grade** | | | < 0.001 |
| I vs. III/IV | 1.486 | 1.438–1.536 | < 0.001 |
| II vs. III/IV | 1.137 | 1.109–1.166 | < 0.001 |
| **T stage** | | | < 0.001 |
| T1a vs. T2 | 1.805 | 1.729–1.884 | < 0.001 |
| T1b vs. T2 | 2.487 | 2.409–2.568 | < 0.001 |
| T1c vs. T2 | 1.869 | 1.825–1.915 | < 0.001 |
| **N stage** | | | < 0.001 |
| N0 vs. N3 | 1.413 | 1.300–1.537 | < 0.001 |
| N1 vs. N3 | 0.985 | 0.905–1.072 | 0.725 |
| N2 vs. N3 | 1.109 | 1.007–1.223 | 0.036 |
| **ER** | | | < 0.001 |
| Negative vs. positive | 0.874 | 0.843–0.906 | < 0.001 |
| **PR** | | | < 0.001 |
| Negative vs. positive | 0.844 | 0.819–0.870 | < 0.001 |
| **Chemotherapy** | | | < 0.001 |
| No or unknown vs. Yes | 0.701 | 0.684–0.719 | < 0.001 |

BCT, breast-conserving therapy; OR, odds ratio; CI, confidence interval; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; ER, estrogen receptor; PR, progesterone receptor.
being diagnosed with primary T1-T2 invasive ductal carcinoma (IDC) or invasive lobular carcinoma (ILC) between 2000 and 2015. Patients over 80 years old; with breast cancer located in the nipple-areolar complex or axillary tail; Tis or T1 mic; with more than one primary cancer; having metastasis at diagnosis; initially identified at death or autopsy only; with unknown information on essential parameters; or missing in follow-up were excluded from the study. Asian, Pacific Islander, American Indian, and Alaska native were regarded as other races. Borderline ER or PR status was considered unknown status. Informed consent was not required because personally identifiable information was not accessed. Institutional Review Board permission was not required because the SEER database is a deidentified national database.

2.2. Statistical Analysis. Demographic information and clinical characteristics were compared using Chi-square tests. Continuous variables were converted to categorical variables using X-tile software (Version 3.6.1) [9]. Multivariable logistic regression was utilized to evaluate the relationship between predictive variables and treatment choice. We used the Kaplan–Meier curve to estimate survival outcomes, and the log-rank test was used to perform between-group comparisons. The Cox proportional hazards model was performed to fit demographic and clinical characteristics for overall survival (OS) and breast cancer-specific survival (BCSS). A 1:1 ratio propensity score matching (PSM) method with a caliper of 0.02 was performed to alleviate the influence of baseline differences on survival outcomes in CLBC and upper-outer breast cancer (UOBC) patients who underwent BCT. Matching variables included the year of diagnosis, age, race, histological type,
# Table 3: Multivariate survival analysis of prognostic factors among BC patients.

|                          | Cox-OS HR (95% CI) | p-value | Cox-BCSS HR (95% CI) | p-value | Fine–Gray CS HR (95% CI) | p-value | CS HR (95% CI) | p-value |
|--------------------------|--------------------|---------|----------------------|---------|--------------------------|---------|----------------|---------|
| **Year of diagnosis**    |                    |         |                      |         |                          |         |                |         |
| 2000–2003 vs. 2008–2015  | 1.427 (1.382–1.472) | < 0.001 | 1.914 (1.832–1.999)  | < 0.001 | 1.607 (1.539–1.678)  | < 0.001 | 1.557 (1.491–1.625) | < 0.001 |
| 2004–2007 vs. 2008–2015  | 1.196 (1.158–1.234) | < 0.001 | 1.329 (1.272–1.389)  | < 0.001 | 1.226 (1.173–1.282)  | < 0.001 | 1.202 (1.150–1.258) | < 0.001 |
| **Age, years**           |                    | < 0.001 |                      |         |                          |         |                |         |
| 64–72 vs. 18–63          | 2.388 (2.318–2.459) | < 0.001 | 1.595 (1.525–1.667)  | < 0.001 | 1.291 (1.227–1.359)  | < 0.001 | 1.318 (1.255–1.384) | < 0.001 |
| 73–79 vs. 18–63          | 4.891 (4.744–5.043) | < 0.001 | 2.877 (2.730–3.033)  | < 0.001 | 1.662 (1.574–1.755)  | < 0.001 | 1.955 (1.855–2.061) | < 0.001 |
| **Race**                 |                    | < 0.001 |                      |         |                          |         |                |         |
| Black vs. white          | 1.378 (1.329–1.429) | < 0.001 | 1.343 (1.279–1.411)  | < 0.001 | 1.291 (1.227–1.359)  | < 0.001 | 1.318 (1.255–1.384) | < 0.001 |
| Others vs. white         | 0.711 (0.677–0.748) | < 0.001 | 0.762 (0.712–0.815)  | < 0.001 | 0.800 (0.747–0.856)  | < 0.001 | 0.788 (0.737–0.843) | < 0.001 |
| **Histology type**       |                    |         |                      |         |                          |         |                |         |
| ILC vs. IDC              | 0.906 (0.864–0.949) | < 0.001 | —                    |         | —                        |         | 0.278 (—)      | —       |
| **Laterality**           |                    |         |                      |         |                          |         |                |         |
| Right vs. Left           | 0.967 (0.944–0.990) | 0.005   | 0.946 (0.915–0.979)  | 0.002   | 0.947 (0.915–0.981)  | 0.002   | 0.946 (0.914–0.979) | 0.001   |
| **Grade**                |                    |         |                      |         |                          |         |                |         |
| II vs. I                 | 1.180 (1.139–1.223) | < 0.001 | 0.958 (0.821–1.107)  | < 0.001 | 1.943 (1.807–2.089)  | < 0.001 | 1.951 (1.813–2.100) | < 0.001 |
| III/IV vs. I             | 1.430 (1.374–1.488) | < 0.001 | 2.719 (2.521–2.933)  | < 0.001 | 2.676 (2.480–2.888)  | < 0.001 | 2.703 (2.505–2.916) | < 0.001 |
| **T stage**              |                    |         |                      |         |                          |         |                |         |
| T1b vs. T1a              | 1.240 (1.161–1.325) | < 0.001 | 1.225 (1.070–1.402)  | 0.003   | 1.175 (1.027–1.344)  | 0.019   | 1.191 (1.041–1.363) | 0.011   |
| T1c vs. T1a              | 1.565 (1.471–1.666) | < 0.001 | 2.177 (1.924–2.464)  | < 0.001 | 2.028 (1.792–2.294)  | < 0.001 | 2.084 (1.842–2.359) | < 0.001 |
| T2 vs. T1a               | 2.306 (2.163–2.458) | < 0.001 | 3.779 (3.339–4.278)  | < 0.001 | 3.470 (3.065–3.929)  | < 0.001 | 3.615 (3.193–4.092) | < 0.001 |
| **N stage**              |                    |         |                      |         |                          |         |                |         |
| N1 vs. N0                | 1.496 (1.435–1.540) | < 0.001 | 1.958 (1.880–2.038)  | < 0.001 | 1.923 (1.845–2.004)  | < 0.001 | 1.948 (1.870–2.028) | < 0.001 |
| N2 vs. N0                | 2.617 (2.494–2.746) | < 0.001 | 3.742 (3.529–3.968)  | < 0.001 | 3.565 (3.352–3.792)  | < 0.001 | 3.705 (3.494–3.929) | < 0.001 |
| N3 vs. N0                | 4.340 (4.084–4.611) | < 0.001 | 6.276 (5.854–6.729)  | < 0.001 | 5.985 (5.546–6.459)  | < 0.001 | 6.306 (5.882–6.760) | < 0.001 |
| **ER**                   |                    |         |                      |         |                          |         |                |         |
| Positive vs. negative    | 0.832 (0.800–0.865) | < 0.001 | 0.789 (0.749–0.832)  | < 0.001 | 0.792 (0.749–0.838)  | < 0.001 | 0.790 (0.749–0.833) | < 0.001 |
| **PR**                   |                    |         |                      |         |                          |         |                |         |
| Positive vs. negative    | 0.834 (0.806–0.862) | < 0.001 | 0.716 (0.681–0.752)  | < 0.001 | 0.723 (0.687–0.761)  | < 0.001 | 0.717 (0.683–0.754) | < 0.001 |
| **Treatment**            |                    |         |                      |         |                          |         |                |         |
| BCT vs. mastectomy       | 0.764 (0.745–0.783) | < 0.001 | 0.760 (0.734–0.787)  | < 0.001 | 0.807 (0.779–0.837)  | < 0.001 | 0.784 (0.757–0.812) | < 0.001 |
| **Chemotherapy**         |                    |         |                      |         |                          |         |                |         |
| Yes vs. no or unknown    | 0.779 (0.757–0.803) | < 0.001 | 0.955 (0.916–0.996)  | 0.032   | —                        |         | 0.063 (—)      | 0.928   |

HR, hazard ratio; CI, confidence interval; ILC, invasive lobular carcinoma; IDC, invasive ductal carcinoma; ER, estrogen receptor; PR, progesterone receptor; BCT, breast-conserving therapy.
patients were enrolled for analysis, among whom 118,552 (65.7%) patients received BCT and 63,963 (34.3%) patients underwent mastectomy. The clinical characteristics are displayed in Table 1. Patients between 64 and 72 years old, white patients, patients with the histology of invasive ductal carcinoma (IDC), and patients with less aggressive characteristics including histologic grades I and II, T1 stage, N0 stage, and positive ER and PR status were more inclined to receive BCT. In addition, patients who underwent BCT were less likely to receive chemotherapy. Figure 1 shows the trend of BCT and mastectomy for the indicated patients from 2000 to 2015, and the breast preservation rates fluctuated around 60%.

3. Results

3.1. Baseline Characteristics and the Trend of Breast-Conserving Therapy (BCT) and Mastectomy among Breast Cancer (BC) Patients. According to our inclusion criteria, 180,495 patients were enrolled for analysis, among whom 118,552 (65.7%) patients received BCT and 63,963 (34.3%) patients underwent mastectomy. The clinical characteristics are displayed in Table 1. Patients between 64 and 72 years old, white patients, patients with the histology of invasive ductal carcinoma (IDC), and patients with less aggressive characteristics including histologic grades I and II, T1 stage, N0 stage, and positive ER and PR status were more inclined to receive BCT. In addition, patients who underwent BCT were less likely to receive chemotherapy. Figure 1 shows the trend of BCT and mastectomy for the indicated patients from 2000 to 2015, and the breast preservation rates fluctuated around 60%.

3.2. Predictive Factors of BCT among BC Patients. Variables that were statistically significant ($p < 0.05$) in univariate analysis were enrolled in the multivariate logistic regression model. The multivariate analysis further validated that clinical features including diagnosis between 2004 and 2007, age between 64 and 72, black race, IDC, lower
histologic grade, smaller tumor size, fewer lymph node metastases, positive ER and PR status, and chemotherapy use were independently correlated with BCT compared with mastectomy (Table 2).

3.3. Survival Analysis among BC Patients Treated with BCT or Mastectomy and Subgroup Analysis. The Kaplan–Meier survival curve revealed that patients who received BCT had better overall survival (OS, $p < 0.001$) and breast cancer-specific survival (BCSS, $p < 0.001$) than those who underwent mastectomy (Figures 2(a) and 2(b)). The cumulative incidence function curve also showed that patients undergoing BCT had a lower risk of breast cancer-associated death (Figure 2(c)). Then, we conducted the Cox proportional hazards model and the competing risks models for the multivariate analyses (Table 3). The results obtained from the Cox model indicated that the independent risk factors associated with the OS and BCSS of BC patients included the year of diagnosis, age, race, histological type, histologic grade, T stage, N stage, ER status, PR status, and chemotherapy status. Notably, BCT was found to be a favorable prognostic factor for OS (HR 0.764, 95% CI 0.745–0.783, $p < 0.001$) and BCSS (HR 0.760, 95% CI 0.734–0.787, $p < 0.001$). Similar results were obtained from competing risks models. BCT was still an independent risk factor in the Fine–Gray model (HR 0.807, 95% CI 0.779–0.837, $p < 0.001$) and the CS model (HR 0.784, 95% CI 0.757–0.812, $p < 0.001$). The subgroup analysis further demonstrated that patients treated with BCT had significantly better prognoses than those who received mastectomy in nearly all subgroups, except for patients of other races in the OS model and ILC patients in the BCSS, Fine–Gray, and CS models (Figure 3).

3.4. Differences in Breast Preservation Rate among BC Patients with Distinct Tumor Locations. To detect the breast preservation rate of BC patients with different primary tumor locations, we divided the whole cohort into five subgroups: centrally located breast cancer (CLBC, $n = 12,051$), upper-outer breast cancer (UOBC, $n = 97,517$), upper-inner breast cancer (UIBC, $n = 34,752$), lower-outer breast cancer (LOBC, $n = 20,091$), and lower-inner breast cancer (LIBC, $n = 16,084$). Strikingly, except for CLBC group patients, more than 60% of patients received BCT in the other four locations.
In the CLBC group, the breast-conserving rate of patients was only 48.7% (Figure 4).

### 3.5. Predictive Factors of BCT among CLBC Patients

The clinical characteristics of CLBC patients are shown in Table 4. Patients between 64 and 72 years old, patients of the white race, patients with IDC, and patients with less aggressive characteristics including histologic grades I and II, T1 stage, N0 stage, ER positivity, and PR positivity tended to receive BCT. Similarly, chemotherapy was less likely to be used for patients who underwent BCT.

In the multivariate logistic regression model, features including age between 64 and 72, white race, IDC, histologic grades I and II, T1 stage, N0 stage, ER positivity, and PR positivity tended to receive BCT. Similarly, chemotherapy was less likely to be used for patients who underwent BCT. (Table 5).

### 3.6. Survival Analysis among CLBC Patients Treated with BCT and Mastectomy

The Kaplan–Meier survival curve showed that CLBC patients treated with BCT had enhanced overall survival (OS, p < 0.001) and breast cancer-specific survival (BCSS, p < 0.001) compared with those who underwent mastectomy (Figures 5(a) and 5(b)). Besides, the cumulative incidence function curve showed that CLBC patients who received BCT were less likely to die from breast cancer (Figure 5(c)). Moreover, the Cox proportional hazards model indicated that the year of diagnosis, age, race, histologic grade, T stage, N stage, PR status, and chemotherapy status were independent risk factors associated with the OS and BCSS of CLBC patients. BCT was also found to be a favorable prognostic factor for OS (HR 0.734, 95% CI 0.672–0.802, p < 0.001) and BCSS (HR 0.660, 95% CI 0.576–0.755, p < 0.001).

In competing risks analyses, BCT was still an independent favorable prognostic factor in the Fine–Gray model (HR 0.709, 95% CI 0.617–0.815, p < 0.001) and the CS model (HR 0.686, 95% CI 0.598–0.786, p < 0.001). However, the black race, which was proven to be a risk factor in the Cox model, was nonsignificant in the Fine–Gray model (p = 0.133) and the CS model (p = 0.109) (Table 6).

The subgroup analysis indicated that patients treated with BCT had significantly better OS in almost all subgroups, except for patients of other races. Furthermore, patients who received BCT shared improved BCSS except for patients of black or other races, with ILC, histologic grade I, and T1a stage compared with those who underwent mastectomy. In the competing risks analyses, BCT patients had better prognoses except for those diagnosed between 2000 and 2007, of black or other races, with ILC, histologic grade I, T1a stage, N3 stage, and negative ER status (Figure 6).

### 3.7. Survival Analysis of BCT Patients with Differentially Located Tumors

To further reveal the safety and prognosis of BCT in CLBC patients, we performed survival analyses among patients with tumors located in five distinct areas (Table 7). When compared to UOBC, despite a worse OS
in CLBC, tumors located in these two areas shared a similar BCSS \((p = 0.319)\) and had no significant difference in the Fine–Gray model \((p = 0.578)\) and the CS model \((p = 0.482)\) (Table 7, Table S1). Then, due to the huge differences in the patient number and clinical characteristics, we conducted propensity score matching (PSM) to reduce the influence of confounding factors. After matching, 5,864 patients in each cohort were enrolled. The results showed that patients with CLBC and UOBC had comparable prognoses in all models except the Cox-OS model (Table 7, Table S2). Intriguingly, CLBC patients showed improved prognoses when compared to those with UIBC (Table 7, Table S3), LOBC (Table 7, Table S4), and LIBC (Table 7, Table S5). Subsequently, we performed subgroup analyses among patients with CLBC and those with UIBC (Figure S1), LOBC (Figure S2), and LIBC (Figure S3). Patients in CLBC group showed similar prognoses compared to those with UIBC and LOBC in nearly all subgroups. When compared to LIBC, CLBC patients had better prognoses in most subgroups.

In addition, to explore whether the difference in prognosis between CLBC and LIBC is caused by internal mammary node (IMN) metastasis, we performed a survival analysis among patients without IMN metastasis in these two cohorts. The results indicated that compared to LIBC, CLBC was still an independent favorable prognostic factor among BCT patients (Table S6).

4. Discussion

To the best of our knowledge, this is the first population-based retrospective study using the competing risks model to evaluate the prognosis of TI-T2 CLBC patients undergoing BCT or mastectomy.
Table 6: Multivariate survival analysis of prognostic factors among CLBC patients.

|                     | Cox-OS HR 95% CI | p-value | Cox-BCSS HR 95% CI | p-value | Fine-Gray HR 95% CI | p-value | CS HR 95% CI | p-value |
|---------------------|------------------|---------|--------------------|---------|---------------------|---------|-------------|---------|
| Year of diagnosis   |                  |         |                    |         |                     |         |             |         |
| 2000–2003 vs. 2008–2015 | 1.329 1.194–1.479 | <0.001 | 2.005 1.715–2.344 | <0.001 | 1.629 1.395–1.903 | <0.001 | 1.536 1.315–1.795 | <0.001 |
| 2004–2007 vs. 2008–2015 | 1.134 1.016–1.265 | 0.025 | 1.441 1.226–1.693 | <0.001 | 1.310 1.114–1.541 | 0.001 | 1.267 1.078–1.488 | 0.004 |
| Age, years          |                  |         |                    |         |                     |         |             |         |
| 64–72 vs. 18–63     | 2.437 2.200–2.700 | <0.001 | 1.757 1.514–2.039 | <0.001 | 1.380 1.183–1.609 | <0.001 | 1.482 1.274–1.724 | <0.001 |
| 73–79 vs. 18–63     | 4.904 4.419–5.441 | <0.001 | 3.258 2.763–3.843 | <0.001 | 1.611 1.347–1.927 | <0.001 | 2.004 1.685–2.383 | <0.001 |
| Race                |                  |         |                    |         |                     |         |             |         |
| Black vs. white     | 1.213 1.056–1.393 | <0.001 | 1.263 1.083–1.538 | <0.001 | 1.380 1.183–1.609 | <0.001 | 1.267 1.078–1.488 | 0.004 |
| Others vs. white    | 0.683 0.579–0.805 | <0.001 | 0.703 0.558–0.885 | <0.001 | 0.766 0.606–0.968 | 0.025 | 0.739 0.587–0.931 | 0.100 |
| Histology type      |                  |         |                    |         |                     |         |             |         |
| ILC vs. IDC         |                  |         |                    |         |                     |         |             |         |
| Grade               |                  |         |                    |         |                     |         |             |         |
| II vs. I            | 1.207 1.068–1.364 | <0.001 | 2.616 1.964–3.486 | <0.001 | 2.651 1.993–3.526 | <0.001 | 2.658 1.994–3.542 | <0.001 |
| III/IV vs. I        | 1.436 1.255–1.642 | <0.001 | 3.435 2.567–4.596 | <0.001 | 3.399 2.521–4.583 | <0.001 | 3.426 2.549–4.604 | <0.001 |
| T stage             |                  |         |                    |         |                     |         |             |         |
| T1b vs. T1a         | 1.081 0.866–1.350 | <0.001 | 0.834 0.555–1.254 | 0.384 | 0.838 0.561–1.251 | 0.386 | 0.842 0.560–1.266 | 0.408 |
| T1c vs. T1a         | 1.463 1.194–1.793 | <0.001 | 1.348 0.947–1.920 | 0.097 | 1.262 0.891–1.788 | 0.191 | 1.303 0.913–1.859 | 0.145 |
| T2 vs. T1a          | 2.086 1.697–2.563 | <0.001 | 2.398 1.690–3.403 | <0.001 | 2.196 1.553–3.105 | <0.001 | 2.312 1.625–3.291 | <0.001 |
| N stage             |                  |         |                    |         |                     |         |             |         |
| N1 vs. N0           | 1.455 1.322–1.602 | <0.001 | 1.859 1.613–2.141 | <0.001 | 1.901 1.636–2.209 | <0.001 | 1.939 1.678–2.242 | <0.001 |
| N2 vs. N0           | 2.491 2.129–2.914 | <0.001 | 3.847 3.141–4.712 | <0.001 | 3.776 3.037–4.696 | <0.001 | 3.969 3.231–4.875 | <0.001 |
| N3 vs. N0           | 4.567 3.763–5.541 | <0.001 | 7.081 5.603–8.949 | <0.001 | 6.353 4.897–8.242 | <0.001 | 6.853 5.411–8.680 | <0.001 |
| ER                  |                  |         |                    |         |                     |         |             |         |
| Positive vs. negative | 0.824 0.719–0.945 | 0.005 | — — 0.099 — — 0.099 — | — — 0.344 — | — — 0.214 |
| PR                  |                  |         |                    |         |                     |         |             |         |
| Positive vs. negative | 0.851 0.763–0.949 | 0.004 | 0.625 0.550–0.711 | <0.001 | 0.641 0.543–0.757 | <0.001 | 0.644 0.549–0.755 | <0.001 |
| Treatment           |                  |         |                    |         |                     |         |             |         |
| BCT vs. mastectomy  | 0.734 0.672–0.802 | <0.001 | 0.660 0.576–0.755 | <0.001 | 0.709 0.617–0.815 | <0.001 | 0.686 0.598–0.786 | <0.001 |
| Chemotherapy        |                  |         |                    |         |                     |         |             |         |
| Yes vs. no or unknown | 0.765 0.695–0.843 | <0.001 | — — 0.381 — — 0.809 | 0.699 |

CLBC, centrally located breast cancer; HR, hazard ratio; CI, confidence interval; ILC, invasive lobular carcinoma; IDC, invasive ductal carcinoma; ER, estrogen receptor; PR, progesterone receptor; BCT, breast-conserving therapy.
**Table 6:** Survival outcome in each subgroup among CLBC patients. (a) OS in the Cox proportional hazards model. (b) BCSS in the Cox proportional hazards model. (c) Fine–Gray model in the competing risks analysis. (d) CS model in the competing risks analysis. CLBC, centrally located breast cancer; UIBC, upper-inner breast cancer; LOBC, lower-outside breast cancer; HR, hazard ratio; CI, confidence interval.

**Table 7:** Multivariate survival analysis of prognostic factors among BCT patients with tumor located in the central portion and other quadrants.

**Figure 6:** Survival outcome in each subgroup among CLBC patients. (a) OS in the Cox proportional hazards model. (b) BCSS in the Cox proportional hazards model. (c) Fine–Gray model in the competing risks analysis. (d) CS model in the competing risks analysis. CLBC, centrally located breast cancer; OS, overall survival; BCSS, breast cancer-specific survival; CS, cause specific.
Several clinical trials have shown that patients treated with BCT and mastectomy have equivalent prognoses. For example, the NSABP B-06 trial demonstrated no significant differences in disease-free survival, distant-disease-free survival, or overall survival between early-stage BC patients treated with BCT and mastectomy [1]. The DBCG-82TM trial also showed no significant difference in 10-year recurrence-free survival and 20-year overall survival between these two groups [10]. Several studies even showed improved BCSS and OS for BCT compared with mastectomy [11, 12]. Moreover, BCT also achieved superior cosmetic outcomes than mastectomy [4]. However, our research demonstrated that nearly 40% of early-stage BC patients received mastectomy each year between 2000 and 2015, and this proportion increased to over 50% in CLBC patients. The hesitation of surgeons performing BCT for CLBC patients may be partially due to the special location or anatomic structure of tumors, including the complex lymphatic drainage [13]. Although a recent retrospective study based on the SEER database discussed the benefit of BCT in CLBC patients, only the classic Cox proportional hazards model was applied, and detailed subgroup analysis was absent [14]. Zhang’s study compared the prognosis of breast-conserving surgery and mastectomy, but the postoperative radiotherapy status was not controlled [8].

In this study, we revealed a higher proportion of IDC, lower histologic grade, T stage and N stage, and positive ER and PR status to receive BCT for BC, including CLBC patients. These factors were mostly associated with a smaller region or less malignant tumor. However, as the SEER database does not collect information on the sequence of chemotherapy and surgery, we could not clarify the influence of neoadjuvant chemotherapy on the choice of BCT or mastectomy. In addition, the status of endocrine therapy and Ki-67, which influence the survival of BC patients, was also unattainable from SEER [15, 16].

Our research demonstrated significantly improved OS and BCSS for BCT in both the whole BC cohort and CLBC alone cohort, which was concordant with previous studies [14, 17, 18]. Importantly, we performed the competing risks models, which take into account not only deaths caused by BC but also deaths caused by other events as well as their effects. We presented the outcomes of two competing risks models: the Fine–Gray model, which is appropriate for evaluating prognostic factors [19], and the CS model, which is more suitable for etiological research [20]. In line with the Cox model, both competing risks models showed better prognoses for BCT, whether in the entire BC cohort or CLBC cohort. These results further proved the safety and efficacy of BCT in the selected population. In addition, patients with ILC showed better survival outcomes than IDC patients, which aligned with earlier studies [21, 22]. When deeply dug, most subgroups of BC could benefit from BCT. All subgroup patients of CLBC showed at least equivalent prognoses receiving BCT compared with mastectomy, and some subgroups such as white race, IDC, lower N stage, and positive ER status could benefit from BCT. Combined with previous studies, patients with these beneficial factors could be more inclined to choose BCT in future clinical decisions [23].

When comparing survival outcomes of BCT in CLBC and other areas, we found that CLBC was comparable with UOBC in the Cox-BCSS model, Fine–Gray model, and CS model after propensity score matching and better than tumors located in the other three quadrants. Some studies have shown that LIBC is an unfavorable prognostic factor for early-stage BC patients, probably due to the higher possibility of IMN metastasis [24, 25]. However, our study showed that CLBC still had a better prognosis than LIBC among patients without IMN metastasis in the BCT cohort.

There are still some limitations in our research. First, we could not evaluate the influence of neoadjuvant chemotherapy on surgical choice and survival outcome. Information on local recurrence rates was also unavailable. Thus, we could not compare local recurrence rates as a secondary outcome between the BCT and mastectomy cohorts. In addition, we could not obtain data about the cosmetic results and satisfaction with body image after BCT. Finally, the status of endocrine therapy, Ki-67, and patients’ income level was absent, which may introduce bias into our results.

In conclusion, utilizing the classic Cox proportional hazards model and competing risks model, our research not only revealed the superiority of BCT compared with mastectomy in most early-stage breast cancer but also proved that patients with CLBC could also obtain better prognoses from BCT.

Data Availability

The datasets analyzed during the current study are available in the SEER database. https://seer.cancer.gov/.

Ethical Approval

This study was performed in line with the principles of the Declaration of Helsinki. Institutional Review Board permission was not required because the SEER database is a deidentified national database.

Consent

Informed consent was not required because personally identifiable information was not accessed.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Authors’ Contributions

TSY, FM, and BLG designed the study. WLC, TW, YQD, YD, and HYZ collected the data. TSY, ZAC, JYF, ABH, and MCL conducted the statistical analyses. TSY, FM, and YLL collectively conceptualized the manuscript. BLG edited the manuscript and provided critical comments. All authors read and approved the final manuscript.
Acknowledgments

This research was supported by grants from the National Natural Science Foundation of China (81872135 and 82002791) and the Funds for Distinguished Young Scientists of the Second Affiliated Hospital of Harbin Medical University.

Supplementary Materials

Figure S1. Survival outcome in each subgroup among UIIBC and CLBC patients who underwent BCT. (A) OS in the Cox proportional hazards model. (B) BCSS in the Cox proportional hazards model. (C) Fine–Gray model in the competing risks analysis. (D) CS model in the competing risks analysis. UIIBC, upper-inner breast cancer; CLBC, centrally located breast cancer; BCT, breast-conserving therapy; OS, overall survival; BCSS, breast cancer-specific survival; CS, cause specific. Figure S2. Survival outcome in each subgroup among LOBC and CLBC patients who underwent BCT. (A) OS in the Cox proportional hazards model. (B) BCSS in the Cox proportional hazards model. (C) Fine-gray model in the competing risks analysis. (D) CS model in the competing risks analysis. LOBC, lower-outter breast cancer; CLBC, centrally located breast cancer; BCT, breast-conserving therapy; OS, overall survival; BCSS, breast cancer-specific survival; CS, cause specific. Figure S3. Survival outcome in each subgroup among UIBC and CLBC patients who underwent BCT. (A) OS in the Cox proportional hazards model. (B) BCSS in the Cox proportional hazards model. (C) Fine–Gray model in the competing risks analysis. (D) CS model in the competing risks analysis. UIBC, upper-inner breast cancer; CLBC, centrally located breast cancer; BCT, breast-conserving therapy; OS, overall survival; BCSS, breast cancer-specific survival; CS, cause specific. Table S1. Multivariate survival analysis of prognostic factors among UIIBC and CLBC patients who underwent BCT in the whole cohort. Table S2. Multivariate survival analysis of prognostic factors among UIIBC and CLBC patients who underwent BCT in the matched cohort. Table S3. Multivariate survival analysis of prognostic factors among UIBC and CLBC patients who underwent BCT. Table S4. Multivariate survival analysis of prognostic factors among LOBC and CLBC patients who underwent BCT. Table S5. Multivariate survival analysis of prognostic factors among LOBC and CLBC patients who underwent BCT. Table S6. Multivariate survival analysis of prognostic factors among UIBC and CLBC patients with negative IMN who underwent BCT. (Supplementary Materials)

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