Breast conserving therapy for central breast cancer in the United States

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Abstract

Introduction: Although central breast cancer is not a contraindication to breast conserving, most surgeons still choose to perform total mastectomy. The safety of breast conserving treatment for central breast cancer is still unclear. The purpose of this study is to evaluate the long-term survival outcome of central breast cancer.

Materials and methods: Using SEER database to explore the trend of surgical procedures for patients with central breast cancer. The patients were divided into breast conserving group and non-breast conserving group. Multivariate logistic regression was used to evaluate predictors of breast conserving surgery in central breast cancer. The clinicopathological variables were adjusted through the multivariable Cox risk model, and the stage and T stage were stratified to compare survival results.

Results: A total of 8702 patients with central breast cancer underwent surgical treatment from 2010 to 2015. There were 3870 patients in the breast conserving group and 4832 patients in the non-breast conserving group. The breast preservation rate was 44.4%, which rose from 39.9% in 2010 to 51% in 2015. Elderly patients (p < 0.001) and low tumor malignancy were predictors of breast conserving therapy. In the 1:1 matched case–control analysis, breast cancer-specific survival (BCSS) (p < 0.001) and overall survival (OS) (p < 0.001) in breast conserving therapy group were still higher than those of non-breast conserving. In the subgroup analysis of T staging and stage, the breast conserving therapy group still had higher OS and BCSS.

Conclusion: In central breast cancer, breast-conserving therapy is safe and optional.

Keywords: Central breast cancer, Nipple-areola complex, Breast conserving therapy, Overall survival, Breast cancer-specific survival

Introduction
Breast conserving therapy (BCT) allows patients to achieve esthetic outcomes, quality of life and preserve their breast without sacrificing oncologic outcome [1–3] and is considered as a safe treatment for early-stage breast cancer.

Central breast cancer usually refers to tumors located in the area within 2 cm of the nipple-areola complex (NAC). The research on BCT of central breast cancer were few and small sample size though the results showed acceptable recurrence rate of BCT in central breast cancer (4.8–7%) [4–6] and the non-inferior survival outcomes [5, 7, 8] compared with non-BCT. So for central cancers breast conserving therapy was not contraindication in the guideline, but was less likely to be recommended by surgeons for reasons below: (1) careful pathologic examination of mastectomy specimens has found that more than 30% involve the nipple-areola complex [9–11] and lumpectomies that remove the nipple-areola complex often result in poor cosmesis. (2)
Perceived increase in the risk of local recurrence owing to inadequate margins. Recent stunning result was reported from a SEER data based research including 16522 central breast cancer which showed an improved survival rate for centrally located breast cancer (CLBC) receiving BCT [12]. But the early studies on the safety of BCT for CLBC [4, 13–16] or the comparison of oncological outcomes between BCT and non-BCT [7, 8] and the recent SEER based result [12] were all constrained to T1-2 stage without taking T3-4 into account which cannot meet the increasing demand for more cosmetically acceptable breast cancer surgery. Also HER-2 status was an important factors influencing the survival outcome of breast cancer, which was not included in the recent SEER based result. So a study on the survival difference between BCT and non-BCT in central and NAC, especially in T3-4 subgroup population is urgently need.

Materials and methods
Data source and study population
The Surveillance, Epidemiology, and End Results (SEER) database was used to evaluate the safety of breast conserving therapy. We acquired permission to download and analyze data for academic purpose (reference number: 10727-Nov2020). This study does not contain any experiments on humans as well as animals and/or the use of human tissue samples performed by any of the authors. The SEER cancer registries provide population-based cancer surveillance for 17 areas that represent approximately 26% of the United States. Inclusion criteria: (1) the diagnosing year ranged from 2010 to 2015, (2) the primary site of tumor was breast, (3) tumor site was central portion of breast (C50.1) or nipple (C50.0), and (4) patients underwent breast surgery. Exclusion criteria: (1) patients with stage IV disease, (2) patients with unknown information of race, diagnosing year, marital status or important clinicopathological data, (3) patients younger than 18 years old or elder than 80, (4) patients with a history of other cancer, (5) patients with less than 1 month survival after diagnosis, and (6) patient’s diagnoses were only depended on biopsy or autopsy. Finally, a total of 8702 adult breast cancer patients aged 19 to 79 years between 2010 and 2015 was included, and we stratified patients into 2 groups by type of surgery: breast conserving therapy (n = 3870) and non-breast conserving therapy (n = 4832). The non-breast conserving therapy included mastectomy and breast reconstruction.

Statistical analysis
Chi-squared testing was used to compare the differences in baseline characteristics between patients treated with non-BCT versus patients treated with BCT. Multivariable logistic regression was used to identify factors associated with surgery type. Kaplan–Meier analysis was used to compare overall survival outcomes between patients treated with different surgery type. Univariate and Multivariate Cox regression analysis was used to assess potential factors affecting breast cancer-specific survival (BCSS) and overall survival (OS) in patients with central breast cancer. Factors evaluated in the multivariate analysis model included surgery type, age at diagnosis, race, marital status, year at diagnosis, grade, T stage, N stage, ER status, PR status, and HER-2 status. To diminish the effects of baseline differences on outcome differences in the BCT and non-BCT groups, the propensity score matching (PSM) method was applied by matching each BCT case to non-BCT cases. They were exactly matched for the age, race, marital status, grade, T stage, N stage, ER status, PR status and HER-2 status. P < 0.05 was considered as an indicator of statistical significance. SPSS statistics (version 22, IBM, NY) was used to conduct all the above analyses.

Results
The trend of BCT and non-BCT among central breast cancer and relevant clinical characteristics
From 2010 to 2015, a total of 8702 patients met our inclusion criteria and were included for analysis. The study consisted of 3870 (44.4%) patients with BCT and 4832 (55.6%) patients with non-BCT. The clinical characteristics of the BCT and non-BCT groups were summarized in Table 1. BCT was performed more frequently since 2010. Older patients, white patients, married patients, grade II, early stage, T1 stage, N0 stage, ER positive, PR positive, HER-2 negative were more likely to receive BCT, and the proportion of those factors differed significantly between BCT and non-BCT group except for marital status. Comparing patients treated with non-BCT, patients initially treated with BCT were older at diagnosis (P < 0.001), have lower grade (P < 0.001), lower TNM stage (P < 0.001), lower T stage (P < 0.001), lower N stage (P < 0.001) and more likely to be ER positive at diagnosis (P < 0.001), PR positive at diagnosis (P < 0.001) and HER-2 negative at diagnosis (P < 0.001). They are also more likely to be of white race (P < 0.001). Figure 1 showed a trend
of BCT for T1-4 central breast cancer and the BCT rate (51%) exceeded non-BCT in 2015.

Predictive factors of BCT among central breast cancer
The results of multivariate logistic regression are reported in Table 2. Results confirmed that higher T stage (P < 0.001; T2: OR 0.447, 95% CI 0.402–0.496; T3: OR 0.152, 95% CI 0.118–0.195; T4: OR 0.182, 95% CI 0.134–0.247), higher N stage (P < 0.001; N1: OR 0.634, 95% CI 0.570–0.706; N2: OR 0.304, 95% CI 0.242–0.381; N3: OR 0.216, 95% CI 0.150–0.311), positive HER-2 status (P = 0.004; OR 0.822, 95% CI 0.719–0.940) and higher grade (P = 0.014; Grade II: OR 0.843, 95% CI 0.747–0.951; Grade III: OR 0.819, 95% CI 0.707–0.949) were independently associated with non-BCT. Other significant predictors of BCT include higher age (45–59 years: OR 2.026, 95% CI 1.706–2.405; 60–79 years: OR 2.581, 95% CI 2.182–3.053) and years at diagnosis (OR 1.076, 95% CI 1.048–1.106).

Survival significance of BCT among central breast cancer
The Kaplan–Meier survival curve showed that BCT group had better OS and BCS5 than non-BCT group (Fig. 2, both P < 0.001). For patients with central breast cancer, type of surgery, age, race, marital status, years at diagnosis, grade, T stage, N stage, ER status, PR status and HER-2 status were considered as potential prognostic variables and were included in the initial univariate and multivariate models. The results of the univariate analysis proportional hazard regression

Table 1 Comparison of patient and tumor characteristics between the BCT and non-BCT group

|                | BCT group | Non-BCT group | P-value |
|----------------|-----------|---------------|---------|
| No %           | No %      |               |         |
| Years at diagnosis |          |               | <0.001  |
| 2010           | 570 14.70 | 859 17.80     |         |
| 2011           | 598 15.50 | 745 15.40     |         |
| 2012           | 627 16.20 | 868 18.00     |         |
| 2013           | 619 16.00 | 836 17.30     |         |
| 2014           | 681 17.60 | 779 16.10     |         |
| 2015           | 775 20.00 | 745 15.40     |         |
| Age <45        | 249 6.40  | 717 14.80     | <0.001  |
| 45–59          | 1331 34.40| 1861 38.50    |         |
| 60–79          | 2290 59.20| 2254 46.60    |         |
| Race White     | 3165 81.80| 3711 76.80    | <0.001  |
| Black          | 349 9.00  | 474 9.80      |         |
| Others         | 356 9.20  | 647 13.40     |         |
| Marital Married| 2370 61.20| 2911 60.20    | 0.439   |
| Single         | 577 14.90 | 767 15.90     |         |
| Divorced       | 923 23.90 | 1154 23.90    |         |
| Grade Grade I  | 1037 26.80| 780 16.10     | <0.001  |
| Grade II       | 1908 49.30| 2343 48.50    |         |
| Grade III      | 918 23.70 | 1692 35.00    |         |
| Grade IV       | 7 0.20    | 17 0.40       |         |
| Stage Stage I  | 2218 57.30| 1311 27.10    | <0.001  |
| Stage II       | 1439 37.20| 2198 45.50    |         |
| Stage III      | 213 5.50  | 1323 27.40    |         |
| T stage T1     | 2766 71.50| 1924 39.80    | <0.001  |
| T2             | 971 25.10 | 1961 40.60    |         |
| T3             | 79 2.00   | 598 12.40     |         |
| T4             | 54 1.40   | 349 7.20      |         |
| N stage N0     | 2810 72.60| 2266 46.90    | <0.001  |
| N1             | 917 23.70 | 1687 34.90    |         |
| N2             | 107 2.80  | 560 11.60     |         |
| N3             | 36 0.90   | 319 6.60      |         |
| ER status Positive | 434 11.20| 742 15.40     | <0.001  |
| PR status Positive | 3436 88.80| 4090 84.60    | <0.001  |
| HER-2 status Negative | 800 20.70| 1263 26.10    | <0.001  |
| Positive       | 3070 79.30| 3569 73.90    |         |
| Negative       | 3350 86.60| 3889 80.50    | <0.001  |
| Positive       | 520 13.40 | 943 19.50     |         |
identified BCT significantly reduced overall death hazard (HR 0.396; 95%CI 0.332–0.473; P < 0.001) and breast-specific death hazard (HR 0.266; 95%CI 0.206–0.342; P < 0.001) (Tables 3, 4). And BCT still significantly reduced overall death hazard (HR 0.633; 95%CI 0.522–0.766; P < 0.001) and breast-specific death hazard (HR 0.570; 95%CI 0.435–0.746; P < 0.001) in the adjust multivariate Cox analysis. Other factors including age (P < 0.001), race (P < 0.001), marital status (P < 0.001), years at diagnosis (P = 0.038), grade (P < 0.001), T stage (P < 0.001), N stage (P < 0.001), ER status (P = 0.003), PR status (P < 0.001) and HER-2 status (P = 0.039) were identified as independent significant predictors of T1-4 central breast cancer overall mortality (OM), and race (P < 0.001), marital status (P = 0.007), grade (P < 0.001), T stage (P < 0.001), N stage (P < 0.001), ER status (P = 0.005), PR status (P < 0.001) and HER-2 status (P = 0.008) were identified as independent significant predictors of central breast cancer breast-specific mortality (BCSM).

BCT as a prognostic factor for survival after propensity score matching
To further corroborate the findings from univariable and multivariable proportional hazard regression, a propensity score-adjusted analysis was performed. A total of 2757 patients who underwent BCT were matched to 2757 patients who underwent non-BCT. Within the post-propensity cohort, there was no difference between both groups with regards to age (P = 0.114), race (P = 0.527), marital status (P = 0.287), grade (P = 0.669), T stage (P = 0.722), N stage (P = 0.547), ER status (P = 0.579), PR status (P = 0.409) and HER-2 status (P = 0.458) (Table 5). Using Kaplan–Meier survival estimates, BCT was associated with improved OS (P = 0.001) (Fig. 3) in the post-propensity cohort. In the subgroup analysis based on the post-propensity cohort. The beneficial impact of BCT on survival was additionally confirmed stratified for stage, and the P value were 0.018 for stage I, 0.009 for stage II, and 0.004 for stage III (Fig. 4). The BCT group had a higher OS compared with the non-BCT group in T1-2 (P < 0.001) and T3-4 (P = 0.037) (Fig. 5).

Discussion
BCT involves excision of the tumor (lumpectomy) followed by adjuvant whole breast irradiation (WBI). In order to perform BCT, it must be possible to excise the tumor to negative margins with an acceptable cosmetic outcome, the patient must be able to receive radiotherapy, and the breast must be suitable for follow-up to allow prompt detection of local recurrence. Landmark trials have established that breast conservation therapy (BCT) and mastectomy offer equivalent survival and can

**Table 2** Multivariate logistic regressions model for predictors of breast conserving therapy

| Factor          | OR   | 95% CI       | P-value |
|-----------------|------|--------------|---------|
| Age             |      |              | <0.001  |
| < 45            | 1    | Reference    |         |
| 45–59           | 2.026| 1.706–2.405  | <0.001  |
| 60–79           | 2.581| 2.182–3.053  | <0.001  |
| Race            |      |              | <0.001  |
| White           | 1    | Reference    |         |
| Black           | 1.030| 0.874–1.213  | 0.725   |
| Others          | 0.680| 0.585–0.79   | <0.001  |
| Marital         |      |              | 0.059   |
| Married         | 1    | Reference    |         |
| Single          | 1.146| 1.001–1.313  | 0.049   |
| Divorced        | 0.952| 0.850–1.067  | 0.4     |
| Year of diagnosis | 1.076| 1.048–1.106  | <0.001  |
| Grade           |      |              | 0.014   |
| Grade I         | 1    | Reference    |         |
| Grade II        | 0.843| 0.747–0.951  | 0.005   |
| Grade III       | 0.819| 0.707–0.949  | 0.008   |
| Grade IV        | 0.477| 0.182–1.251  | 0.132   |
| T stage         |      |              | <0.001  |
| T1              | 1    | Reference    |         |
| T2              | 0.447| 0.402–0.496  | <0.001  |
| T3              | 0.152| 0.118–0.195  | <0.001  |
| T4              | 0.182| 0.134–0.247  | <0.001  |
| N stage         |      |              | <0.001  |
| N0              | 1    | Reference    |         |
| N1              | 0.634| 0.57–0.706   | <0.001  |
| N2              | 0.304| 0.242–0.381  | <0.001  |
| N3              | 0.216| 0.150–0.311  | <0.001  |
| ER status       |      |              | 0.987   |
| Negative        | 1    | Reference    |         |
| Positive        | 1.002| 0.829–1.209  | 0.987   |
| PR status       |      |              | 0.082   |
| Negative        | 1    | Reference    |         |
| Positive        | 1.141| 0.984–1.323  | 0.082   |
| HER-2 status    |      |              | 0.004   |
| Negative        | 1    | Reference    |         |
| Positive        | 0.822| 0.719–0.94    | 0.004   |
be viewed as equivalent treatments in early stage breast cancer (ESBC) [17, 18]. Breast conserving therapy followed by radiotherapy allows patients to achieve esthetic outcomes, quality of life and preserve their breast without sacrificing oncologic outcome [1–3] and is considered as a safe treatment for early-stage breast cancer.

The term subareolar defined differently: Fowble et al. [7] and Haffty et al. [6] defined it as the area within 2 cm of the NAC, Haagensen shrank the distance to only 1 cm, and Simmons et al. [5] defined it as the area immediately beneath the areola. Central tumors usually refer to subareolar with some exceptions: only include NAC [19], tumors > 2 cm from areolar margin [7]. NAC malignant tumors included Paget disease, lymphoma and invasive and noninvasive breast cancers [20] and Paget disease were also a candidate for BCT [21]. In our study NAC account for 6.42% (559/8702) central and NAC patients, and the type of surgery did not correlated with location significantly (p = 0.692). But to date, the research on BCT of the NAC breast cancer is limited, so NAC breast cancer were included for further study. The early studies on the safety of BCT for CLBC [4, 13–16] or the comparison of oncological outcomes between BCT and non-BCT [7, 8] and the recent SEER based result [12] were all constrained to T1–2 stage. In our logistic analysis, we found that there is a significantly lower proportion of a young age (< 45 years old) in BCT group (6.40%) compared with non-BCT group (14.8%). With the popularization of BRCA1/2 genetic testing and the maturity of breast reconstruction surgery, more and more young women are choosing breast reconstruction and contralateral prophylactic mastectomy [25, 26]. This may be why more young women are not opting for breast conserving surgery.

The evidence for breast conserving surgery has expanded with the availability of more drugs and improved efficacy of neoadjuvant therapy. Breast conserving surgery is not limited to early stage, such as T1–T2, but can be extended to T3–T4. In our research, the OS rate of central breast cancer patients was higher with breast conserving surgery than with mastectomy, which was consistent with Zhang’s results [12]. However, our study demonstrates that T3–T4 and stage III patients receiving breast conserving therapy also had higher OS (P < 0.05).

And BCT significantly reduced overall death hazard (HR 0.633; 95%CI 0.522–0.766; P < 0.001) and
### Table 3  Univariable and multivariable models of overall mortality in central breast cancer patients

|                                | Univariate analysis | Multivariate analysis |
|--------------------------------|---------------------|-----------------------|
|                                | HR (95%CI)          | P-value               | HR (95%CI)          | P-value               |
| Surgery type                   |                     |                       |                     |                       |
| Non-BCT                        | Reference            | <0.001                | Reference            | <0.001                |
| BCT                            | 0.396 (0.332–0.473)  | <0.001                | 0.633 (0.522–0.766)  | <0.001                |
| Age                            |                     |                       |                     |                       |
| < 45                           | Reference            | <0.001                | Reference            | <0.001                |
| 45–59                          | 1.029 (0.769–1.378)  | 0.846                 | 1.188 (0.885–1.595)  | 0.252                 |
| 60–79                          | 1.581 (1.201–2.080)  | 0.001                 | 2.012 (1.518–2.668)  | <0.001                |
| Race                           |                     |                       |                     |                       |
| White                          | Reference            | <0.001                | Reference            | <0.001                |
| Black                          | 1.922 (1.568–2.356)  | <0.001                | 1.509 (1.222–1.864)  | <0.001                |
| Others                         | 0.630 (0.466–0.851)  | 0.003                 | 0.566 (0.418–0.767)  | <0.001                |
| Marital                        |                     |                       |                     |                       |
| Married                        | Reference            | <0.001                | Reference            | <0.001                |
| Single                         | 1.596 (1.301–1.959)  | <0.001                | 1.366 (1.106–1.686)  | 0.004                 |
| Divorced                       | 1.829 (1.544–2.166)  | <0.001                | 1.465 (1.231–1.742)  | <0.001                |
| Year of diagnosis              | 0.929 (0.877–0.984)  | 0.012                 | 0.941 (0.888–0.997)  | 0.038                 |
| Grade                          |                     |                       |                     |                       |
| Grade I                        | Reference            | <0.001                | Reference            | <0.001                |
| Grade II                       | 1.392 (1.081–1.793)  | 0.01                  | 1.025 (0.792–1.326)  | 0.85                  |
| Grade III                      | 3.189 (2.497–4.071)  | <0.001                | 1.581 (1.211–2.065)  | 0.001                 |
| Grade IV                       | 4.950 (2.004–12.224) | 0.001                 | 2.438 (0.977–6.08)   | 0.056                 |
| T stage                        |                     | <0.001                |                     | <0.001                |
| T1                             | Reference            |                       | Reference            | <0.001                |
| T2                             | 2.288 (1.906–2.747)  | <0.001                | 1.48 (1.214–1.805)   | <0.001                |
| T3                             | 4.055 (3.208–5.126)  | <0.001                | 1.947 (1.498–2.529)  | <0.001                |
| T4                             | 6.933 (5.452–8.817)  | <0.001                | 2.845 (2.169–3.731)  | <0.001                |
| N stage                        |                     | <0.001                |                     | <0.001                |
| N0                             | Reference            |                       | Reference            | <0.001                |
| N1                             | 1.83 (1.525–2.195)   | <0.001                | 1.461 (1.205–1.772)  | <0.001                |
| N2                             | 3.999 (3.214–4.976)  | <0.001                | 2.482 (1.956–3.149)  | <0.001                |
| N3                             | 6.087 (4.802–7.716)  | <0.001                | 3.180 (2.443–4.140)  | <0.001                |
| ER status                      |                     | <0.001                |                     | 0.003                 |
| Negative                       | Reference            |                       | Reference            |                       |
| Positive                       | 0.362 (0.307–0.427)  | <0.001                | 0.692 (0.544–0.880)  | 0.003                 |
| PR status                      |                     | <0.001                |                       |                       |
| Negative                       | Reference            |                       | Reference            |                       |
| Positive                       | 0.407 (0.350–0.475)  | <0.001                | 0.666 (0.536–0.828)  | <0.001                |
| HER-2 status                   |                     | 0.004                 |                       | 0.039                 |
| Negative                       | Reference            |                       | Reference            |                       |
| Positive                       | 1.318 (1.094–1.588)  | 0.004                 | 0.813 (0.668–0.989)  | 0.039                 |
### Table 4  Univariable and multivariable models of breast cancer-specific mortality in central breast cancer patients

|                                 | Univariate analysis | Multivariate analysis |
|---------------------------------|---------------------|-----------------------|
|                                 | HR (95%CI)           | P-value               | HR (95%CI)           | P-value               |
| Surgery type                    | <0.001              |                       | <0.001              |                       |
| Non-BCT                         | Reference            |                       | Reference            |                       |
| BCT                             | 0.266 (0.206–0.342) | <0.001               | 0.570 (0.435–0.746) | <0.001               |
| Age                             | <0.001              |                       | 0.894               |                       |
| <45                             | Reference            |                       | Reference            |                       |
| 45–59                           | 1.131 (0.843–1.518) | 0.411                 | 1.075 (0.79–1.463)  | 0.645                 |
| 60–79                           | 1.904 (1.437–2.524) | <0.001               | 1.069 (0.785–1.455) | 0.672                 |
| Race                            | <0.001              |                       | <0.001              |                       |
| White                           | Reference            |                       | Reference            |                       |
| Black                           | 1.505 (1.218–1.859) | <0.001               | 1.473 (1.137–1.91)  | 0.003                 |
| Others                          | 0.581 (0.429–0.787) | <0.001               | 0.549 (0.374–0.806) | 0.002                 |
| Marital                         | <0.001              |                       | 0.007               |                       |
| Married                         | Reference            |                       | Reference            |                       |
| Single                          | 1.355 (1.097–1.672) | 0.005                 | 1.244 (0.957–1.618) | 0.103                 |
| Divorced                        | 1.478 (1.243–1.758) | <0.001               | 1.43 (1.141–1.792)  | 0.002                 |
| Year of diagnosis               | 0.935 (0.882–0.99)  | 0.022                 | 0.949 (0.881–1.022) | 0.167                 |
| Grade                           | <0.001              |                       | <0.001              |                       |
| Grade I                         | Reference            |                       | Reference            |                       |
| Grade II                        | 1.04 (0.804–1.346)  | 0.763                 | 1.763 (1.109–2.803) | 0.017                 |
| Grade III                       | 1.612 (1.233–2.106) |                       | 3.159 (1.984–5.029) | <0.001               |
| Grade IV                        | 2.439 (0.977–6.091) | 0.056                 | 4.019 (1.179–13.706) | 0.026                 |
| T stage                         | <0.001              |                       | <0.001              |                       |
| T1                              | Reference            |                       | Reference            |                       |
| T2                              | 1.616 (1.329–1.966) | <0.001               | 1.913 (1.441–2.54)  | <0.001               |
| T3                              | 2.241 (1.733–2.897) | <0.001               | 2.798 (1.998–3.919) | <0.001               |
| T4                              | 3.251 (2.487–4.25)  | <0.001               | 4.072 (2.868–5.782) | <0.001               |
| N stage                         | <0.001              |                       | <0.001              |                       |
| N0                              | Reference            |                       | Reference            |                       |
| N1                              | 1.532 (1.264–1.857) | <0.001               | 1.907 (1.465–2.483) | <0.001               |
| N2                              | 2.725 (2.151–3.452) | <0.001               | 3.525 (2.599–4.781) | <0.001               |
| N3                              | 3.518 (2.706–4.573) | <0.001               | 4.546 (3.282–6.297) | <0.001               |
| ER status                       | 0.003               |                       | 0.005               |                       |
| Negative                        | Reference            |                       | Reference            |                       |
| Positive                        | 0.695 (0.546–0.885) | 0.003                 | Reference            |                       |
| PR status                       | <0.001              |                       | <0.001              |                       |
| Negative                        | Reference            |                       | Reference            |                       |
| Positive                        | 0.664 (0.534–0.825) | <0.001               | 0.519 (0.395–0.681) | <0.001               |
| HER-2 status                    | 0.045               |                       | 0.008               |                       |
| Negative                        | Reference            |                       | Reference            |                       |
| Positive                        | 0.818 (0.672–0.995) | 0.045                 | 0.723 (0.569–0.918) | 0.008                 |
breast-specific death hazard (HR 0.570; 95% CT 0.435–0.746; P < 0.001) in the adjust multivariate Cox analysis. When dug deeply, we found that there is a higher proportion of older age, single marital status, more recent years at diagnosis, lower grade, lower T stage, lower N stage, ER positive status, PR positive status and HER-2 negative status to receive BCT for CLBC and those factors were thought to be associated with favored survival outcome. To eliminate the effect of those confounders on prognosis analysis, propensity match score was used. Post-match cohort showed an improved survival in BCT compared with non-BCT in central and NAC tumors.

One limitation of breast conserving surgery for central breast cancer is postoperative aesthetics. In cases of tumor involvement of the nipple-areola complex, the surgeon may remove the nipple-areola complex to ensure a negative margin. This will bring great damage to postoperative breast aesthetics. Overall, nipple areola composite reconstruction will improve patient satisfaction and confidence. With the development of plastic surgery, a variety of methods of nipple areola composite reconstruction can be achieved, including tattooing, using synthetic materials, local flaps, and grafts [27–30]. This will make up for the shortcomings of breast conserving surgery in central breast cancer. Priya et al. demonstrated for patients with central tumor treated with neoadjuvant chemotherapy, many patients may have successfully converted to nipple-areola complex after reevaluation at the end of chemotherapy [31].

On the premise that the tumor safety and aesthetics can be achieved, breast conserving surgery for central breast cancer is a desirable option.

We recognize several limitations of this study. First of all, this study is a retrospective study with inherent flaws. Even though we use the PSM method, there will still be some biases. Secondly, because the patient’s BRCA gene information is not available, it is impossible to evaluate its impact on the breast cancer surgery in the central region. Third, there is no information about postoperative complications, satisfaction and cosmetic results of breast conserving surgery in our study. Finally, the SEER database does not collect socioeconomic and baseline health information, which may be the relationship between surgical methods and survival. In the absence of prospective high-level evidence, our current large-sample retrospective study is of great significance to assess tumor safety, and more prospective studies are needed in the future.

### Table 5: Comparisons of clinicopathological characteristics between the BCT and non-BCT group in 1:1 matched case-control analysis

| Year of diagnosis | Non-BCT No % | BCT No % | P-value |
|-------------------|--------------|----------|---------|
| 2010              | 478 17.30    | 420 15.20 | <0.001  |
| 2011              | 420 15.20    | 426 15.50 |         |
| 2012              | 500 18.10    | 436 15.80 |         |
| 2013              | 480 17.40    | 437 15.90 |         |
| 2014              | 442 16.00    | 483 17.50 |         |
| 2015              | 437 15.90    | 555 20.10 |         |
| Age <45           | 233 8.50     | 244 8.90 | 0.114   |
| 45–59             | 1035 37.50   | 1101 39.90|         |
| 60–79             | 1489 54.00   | 1412 51.20|         |
| Race              |              |          | 0.527   |
| White             | 2202 79.90   | 2169 78.70|         |
| Black             | 254 9.20     | 274 9.90 |         |
| Others            | 301 10.90    | 314 11.40|         |
| Marital           |              |          | 0.287   |
| Married           | 1713 62.10   | 1671 60.60|         |
| Single            | 405 14.70    | 446 16.20|         |
| Divorced          | 639 23.20    | 640 23.20|         |
| Grade             |              |          | 0.669   |
| Grade I           | 585 21.20    | 569 20.60|         |
| Grade II          | 1360 49.30   | 1406 51.00|         |
| Grade III         | 805 29.20    | 775 28.10|         |
| Grade IV          | 7 0.30       | 7 0.30   |         |
| T stage           |              |          | 0.722   |
| T1                | 1692 61.40   | 1676 60.80|         |
| T2                | 918 33.30    | 948 34.40|         |
| T3                | 85 3.10      | 79 2.90  |         |
| T4                | 62 2.20      | 54 2.00  |         |
| N stage           |              |          | 0.547   |
| N0                | 1760 63.80   | 1799 65.30|         |
| N1                | 843 30.60    | 815 29.60|         |
| N2                | 108 3.90     | 107 3.90 |         |
| N3                | 46 1.70      | 36 1.30  |         |
| ER status         |              |          | 0.579   |
| Negative          | 375 13.60    | 360 13.10|         |
| Positive          | 2382 86.40   | 2397 86.90|         |
| PR status         |              |          | 0.409   |
| Negative          | 636 23.10    | 662 24.00|         |
| Positive          | 2121 76.90   | 2095 76.00|         |
| HER-2 status      |              |          | 0.458   |
| Negative          | 2316 84.00   | 2337 84.80|         |
| Positive          | 441 16.00    | 420 15.20|         |
Fig. 3 Kaplan–Meier survival curves of overall survival and breast cancer-specific survival stratified by BCT and non-BCT in matched case–control analysis (A: OS; B: BCSS)

Fig. 4 Kaplan–Meier survival curves of overall survival for BCT and non-BCT stratified by the stage in matched case–control analysis (A: stage I; B: stage II; C: stage III)

Fig. 5 Kaplan–Meier survival curves of overall survival for BCT and non-BCT stratified by the T stage in matched case–control analysis (A: T1–2; B: T3–4)
Conclusion

There is an increased incidence of BCT in patients with central breast cancer. Old age and low tumor malignancy were predictors of BCT. BCT is a safe and feasible surgical procedure for central breast cancer.

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Authors’ contributions

Conception and design: JL and XZ; Development of methodology: JL, XZ, HH, SL, and CX; Acquisition of data, analysis and interpretation of data (e.g., statistical analysis; biostatistics, computational analysis): JL, XZ, CX; Writing, review and/or revision of the manuscript: JL, XZ and CX; Study supervision: JL and SL; Revising: JL, XZ and CX; All of the authors reviewed, read and approved the final manuscript.

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Availability of data and materials

These data were publicly available for use in accordance with a limited use agreement for SEER research data: Surveillance, Epidemiology, and End Results (SEER) Program (https://seer.cancer.gov) SEER*Stat Database.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). We have obtained permission to access research data files in the SEER program of the National Cancer Institute (reference number 10727-Nov2020). The analysis dataset was extracted without any identifiable information. Thus, informed consent has been waived. Ethical approval has been exempt from review by the Ethics Committee of Fujian Medical University Union Hospital, as SEER database is publicly available and without specific identifiers.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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