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Trends and survival benefits of bilateral breast-conserving surgery in patients with metachronous bilateral breast cancer

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Abstract

Background This study aims to investigate the temporal trends and survival outcomes of bilateral breast-conserving surgery (BCS) in women diagnosed with metachronous bilateral breast cancer (MBBC) in the USA from 2000 to 2019.

Methods Patients with stage T0-T3 and stage 0-III MBBC who underwent unilateral BCS on one side and different surgical procedures on the contralateral side from 2000 to 2019 were identified from the Surveillance, Epidemiology, and End Results (SEER) database. The Cochrane-Armitage test for trend was employed to assess the trends in contralateral breast surgical procedures, including BCS, mastectomy (M) and breast-reconstruction (BR). Overall survival (OS) and breast cancer-specific survival (BCSS) were analyzed using Kaplan-Meier curves and univariate and multivariate Cox proportional hazards regression analyses. Since BR is typically performed following M, survival data for the BR and M groups were combined and collectively analyzed as the M group.

Results A total of 9571 patients with stage T0-T3 and stage 0-III who underwent unilateral BCS were included in this study, with 75.84% ($n=7,259$) opting for BCS treatment. The proportion of BCS was decreased significantly from 90.79% in 2000 to 74.04% in 2019 ($P<0.0001$). Older age was positively correlated with BCS, while recent diagnosis, late T stage, lymph node metastasis, invasive lobular carcinoma and chemotherapy were negatively correlated with BCS. Kaplan-Meier survival analysis indicated that BCS patients had better OS ($P<0.001$) and BCSS ($P<0.001$) compared with patients receiving M. Univariate Cox analysis indicated that BCS showed significant statistical differences in both OS and BCSS. Specifically, the hazard ratio (HR) for OS and BCSS were 0.717 (95% CI 0.649–0.791, $P<0.001$) and 0.484 (95% CI 0.422–0.556, $P<0.001$), respectively. Multivariate Cox analysis indicated that BCS was not an independent prognostic factor for OS (HR = 1.012, 95% CI 0.904–1.132, $P>0.05$), suggesting no significant difference in OS between the BCS and M groups. Conversely, BCS was an independent favorable prognostic factor for BCSS (HR = 0.746, 95% CI 0.634, 0.877; $P<0.05$).

Conclusion Despite the initial high utilization of BCS in MBBC patients, our study revealed a decline in its usage over the course of the study period. Importantly, this decrease did not impact OS, suggesting the safety of BCS for MBBC patients. In light of these findings, clinicians are encouraged to recommend BCS for eligible MBBC patients, emphasizing its viability as a treatment option.

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Keywords Metachronous bilateral breast cancer, Breast-conserving surgery, Prognosis, Trend, Survival

Introduction

Global cancer statistics for 2020 show that breast cancer has surpassed lung cancer to become the highest incidence of malignant tumors in women worldwide and the incidence is increasing year by year [1]. Breast cancer is the most prevalent cancer among women in the United States, constituting 31% of female cancer cases [2]. It ranks as the second leading cause of cancer-related deaths in women, following lung cancer [3, 4]. In the United States, breast cancer is estimated to account for 15.2% of all new cancer cases and 7.1% of cancer-related deaths up to 2023 [5]. The incidence of bilateral breast cancer (BBC) is on the rise, ranging from 1.4 to 11.8% of all breast cancer cases, possibly due to advancements in breast cancer understanding, diagnostics, treatment modalities, and increased life expectancy [6, 7]. A previous study found that approximately 3.4% of patients with unilateral breast cancer (UBC) developed contralateral breast cancer over a 10-year period, with an annual risk of 0.37% over a 25-year period and an actuarial risk of 9.9% over the same period. The risk varies slightly based on several factors such as age at diagnosis, time since diagnosis, and current age [8]. Notably, individuals with BRCA1 or BRCA2 mutations experience a higher prevalence of BBC, with a 10-year risk ranging from 13 to 40%. However, most BBC cases cannot be explained by BRCA mutations alone [9].

At present, there is some controversy about the prognosis of BBC, with some studies suggesting worse outcomes for synchronous bilateral breast cancer (SBBC) compared to UBC. However, research indicates no significant difference in 3-year Overall survival (OS) rates between SBBC and MBBC [8] Moreover, a recent study found that compared with MBBC patients, SBBC patients have a significantly higher prevalence of breast cancer family history and a poorer prognosis [10]. Another study has also found no difference in 3-year OS, disease-free survival and local area control rates between SBBC and MBBC [11].

The optimal surgical treatment for BBC remains uncertain, with suggestions that it should align with strategies for UBC [12]. Mastectomy (M) is commonly used for SBBC and MBBC, with a preference for bilateral breast-conserving surgery (BCS) in MBBC. In Jiang et al.' s study, it was found that M was the most common surgical method used to treat SBBC and MBBC, and about 14% of patients chose contralateral BCS, but MBBC (11.11%) patients appeared to prefer bilateral BCS than SBBC (7.14%) [9]. According to the O'Brien study [13], 57% of patients diagnosed with heterochronous breast cancer underwent BCS at the initial diagnosis. In contrast, only 34% of patients with concurrent breast cancer opted for BCS. Notably, the study found that the estimates for 5-year and 10-year OS were excellent and comparable between both groups. Nevertheless, current prognostic studies on SBBC and MBBC are limited to an examination of OS, with no dedicated investigation into the prognosis of SBBC or MBBC based on various surgical procedures. Hence, there is a compelling need to explore the impact of specific surgical interventions on the prognosis of BBC.

Since patients with MBBC are more inclined to opt for BCS again when breast cancer arises on the contralateral side after having undergone BCS previously, it implies that BCS was operated for MBBC patients on different occasions. Given the lack of conclusive research on whether the prognosis of this approach aligns with that of UBC, our study focuses on the outcomes of bilateral BCS in MBBC. Currently, there is limited evidence on the impact of bilateral BCS on the survival of this distinct patient population. The absence of guidelines for bilateral BCS in the context of MBBC underscores the need for high-quality evidence to determine its benefits to patient survival. Our study aims to contribute valuable insights, enabling MBBC patients to make more informed decisions regarding their choice of operation.

Our study is one of the largest endeavors to assess OS and breast cancer-specific survival (BCSS) of T0-T3 and 0-III MBBC patients who have undergone bilateral BCS based on the Surveillance, Epidemiology and End Results (SEER) database. We examined the time trends associated with unilateral BCS and different contralateral breast surgery methods in MBBC patients over the past two decades.

Methods

Data source and study population

BBC can be divided into SBBC and MBBC according to the time interval between the first and second tumor diagnosis. However, this interval varies greatly across studies. SBBC is defined as two tumors diagnosed 1 month [14],2 months [15],3 months [7],6 months [16], or 1 year [17]. In this study, we adopted a common criterion from previous research, using a 6-month interval as the threshold to distinguish between SBBC and MBBC. This approach aligns with the methodology employed in other studies, such as the work by Baretta et al., where a 6-month interval criterion was relatively more commonly utilized [18]. Specifically, a time interval exceeding 6 months was considered for the identification of MBBC, while a timeframe of less than 6 months was applied to define SBBC [9].

In this study, data were acquired from the SEER database using SEER*Stat software, specifically from the "Incidence. SEER Research Plus Limited-Field Data, 22 Registries, November 2021 Submission [2000–2019]" dataset. Follow-up data were also retrieved from the SEER, with the endpoint of follow-up set at December 31, 2019. Since the inception of surgery codes in the SEER in 2000, we identified women diagnosed with histologically confirmed BBC between 2000 and 2019. To ensure consistency, the study cohort was then refined to patients with invasive ductal or lobular carcinoma, confirmed by histologic codes (ICDO-3 codes 8500/3, 8520/3, and 8522/3). From an initial pool of 39,553 BBC cases, we calculated 19,734 cases of MBBC and 19,819 cases of SBBC. Patients were excluded if they had not undergone surgery or had an unknown type of surgery, had unknown laterality at diagnosis, had no record of nodule status, were lost to follow-up, had metastases, were locally advanced, had a diagnosis of a third or more primary cancer, or had local or distant recurrence before the diagnosis of contralateral breast cancer. A total of 16,325 MBBC cases were identified. Specifically, the number of patients who received unilateral BCS of the first side breast and different surgical methods of the second side was 10,187, the number of patients who received M of the first side breast and different surgical methods of the second side was 5244, and the number of patients who received reconstruction of the first side breast and different surgical methods of the second side was 894. According to the criteria of BCS, the data of stage IV, unknown tumor stage, T4, unknown tumor size, and pathological type of inflammatory breast cancer were excluded. The final number of included cases was 9571. The flowchart is shown in Fig. 1. Survival analysis was performed on these patients. The access to and use of SEER data did not require informed patient consent. Thus, ethical approval was exempted by the Institutional Review Board of Hospital, and the study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [19].

Surgical patterns

Surgical interventions were categorized as BCS, M and breast reconstruction (BR). M included SEER codes for 'total (simple) mastectomy NOS', 'modifed radical mastectomy', 'radical mastectomy NOS', 'extended radical mastectomy', or 'mastectomy NOS'. BR was defined by the SEER code for "breast reconstruction," encompassing various tissue types. BCS was defined by SEER codes for 'partial mastectomy' or 'less than total mastectomy NOS', covering procedures such as lumpectomy, excisional biopsy, re-excision, and segmental mastectomy. The specific surgical codes used were as follows: 20–24 for BCS, 30, 40, 41, 50–52, 60, 70–72, and 80 for M, and 43–49, 53–59, 63–69, and 73–75 for BR. SEER rules mandated the abstraction of each breast as a separate primary when a second primary was found in the contralateral breast, with the surgical code reflecting the unilateral procedure performed on that site. In breast cancer surgery, a gross mastectomy involves removing the entire breast, which typically includes the breast itself, axillary or sentinel lymph nodes, and other surrounding tissues that may impact the surgery's outcome. BR on the other hand, focuses on reshaping the breast's form and appearance. This is achieved by either implanting implants or utilizing fat and tissue from other parts of the patient's body for tissue reconstruction following M. The primary aim of M is to eliminate tumor cells, while reducing the risk of recurrence and improving the OS rate. Meanwhile, the goal of BR is to enhance the patients' quality of life through tissue reconstruction, all while eliminating tumor cells. This allows patients to better adapt to social life after the surgery. Interestingly, there is currently no literature evidence demonstrating whether M alone or in combination with BR significantly affects the recurrence, metastasis, and OS of breast cancer patients. Due to this lack of evidence, the M and BR groups are often combined in follow-up survival analyses, collectively referred to as the M group.

Key variables

Patient demographics included age at diagnosis, year of diagnosis, race, marriage status. Clinicopathological characteristics included tumor grade, histology, T classification, lymph node status, stage, estrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor 2 (HER2) status and previous cancer diagnosis. Permissions were obtained to access SEER program custom data with additional treatment fields such as radiation therapy and chemotherapy. Race was categorized as white, black, other. Marriage status was delineated as married, unmarried (including divorced, separated, unmarried or domestic partner, single, or widowed), and unknown. Tumor grade was classified as I/II (Grade I, well differentiated, differentiated, NOS; Grade II, moderately differentiated, intermediate differentiation), III/IV (Grade III, poorly differentiated; Grade IV, undifferentiated; anaplastic) and unknown. Tumor histology was categorized as ductal, lobular, and other, based on ICDO-3 codes. Those with borderline ER/PR status were considered unknown ER/PR status and those with missing or borderline HER2 status (diagnosed before 2010) were categorized as unknown HER2 status.

Statistical analysis

The rates of surgical patterns over the study period were compared using the Cochrane-Armitage test for trend. Logistic regression model was used to determine the predictors of BCS. The Chi-squared test was used to

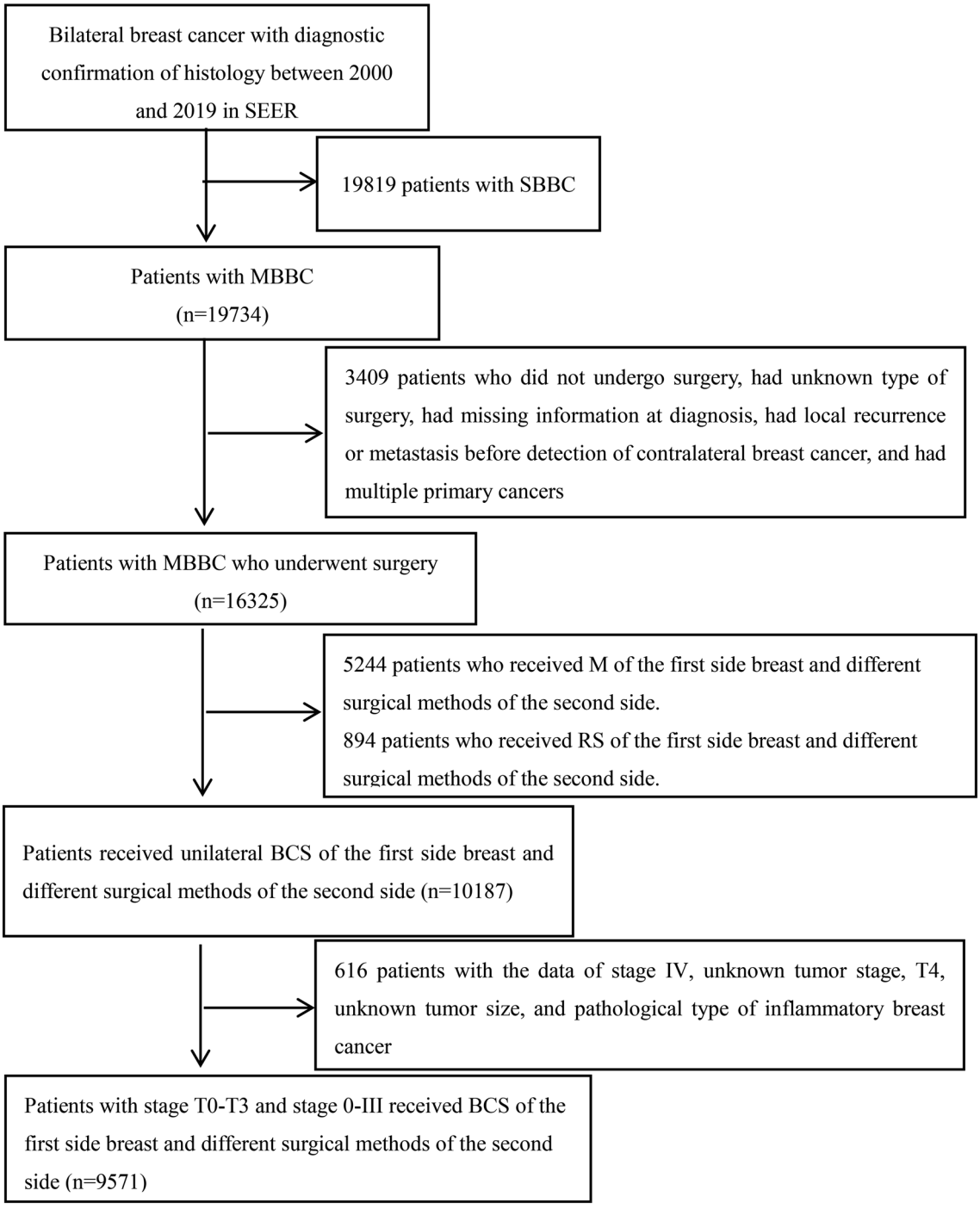

Fig. 1 Study population. SEER: surveillance, epidemiology, and end results, ICDO-3: International classification of diseases for oncology, third edition, M: mastectomy, BCS: breast-conserving surgery, BR: breast-reconstruction, MBBC: metachronous bilateral breast cancer, SBBC: synchronous bilateral breast cancer

compare categorical variables between the BCS, M and BR groups. Given that the influential factors in our analysis primarily consist of counting or ordered data, there is no imperative for data standardization. Hence, the Mann-Whitney U test was employed for analyzing continuous variables. Since BR is typically performed following M, the BR and M groups were combined into a single M group for subsequent survival analyses. Kaplan–Meier curve and univariate/multivariable Cox proportional hazards regression analyses were performed to compare OS and BCSS between BCS and M patients. HER2 status was excluded from predictive factor and survival analysis

due to its unavailability in the SEER database before 2010. A two-sided $P<0.05$ indicated a significant difference. All analyses were executed, and figures were plotted using R statistical software (version 4.1.3).

Results

Baseline characteristics

As illustrated in Fig. 1, a total of 9571 patients diagnosed with stage T0-T3 and stage 0-III underwent unilateral BCS on one side, with varying surgical approaches employed on the contralateral side for the management of MBBC from 2000 to 2019. Among these patients, 75.84% ($n=7259$) opted for BCS treatment, 16.13% ($n=1544$) underwent M treatment, and 8.03% ($n=768$) underwent BR. Significant differences in the distribution of surgical treatments were observed when stratifying the groups based on age. Notably, the rate of BCS increased with advancing age. Table 1 provides an overview of the baseline characteristics of patients based on the type of surgery they received.

Trends in surgical treatments over time

Between 2000 and 2019, the incidence of BCS decreased from 90.79 to 74.04% ($P<0.001$). In contrast, the incidence of M increased from 7.18 to 17.11% ($P<0.001$), and the incidence of BR increased from 2.07 to 8.85% ($P<0.001$; Fig. 2). The BCS usage was high in 2000, but over time, the usage of BCS gradually declined, while the usage of M and BR gradually increased. Significant linear trends with time were evident in all the three groups. From 2000 to 2019, the proportion of patients under 50 who underwent BCS on the other side decreased from 100 to 25%. In contrast, the utilization rates of M increased from 0 to 40.62% ($P<0.001$), and BR rates increased from 0 to 34.38% ($P<0.001$) (eFigure 1 in Supplement). A similar trend was observed in patients aged 50–64 years and over 65 years (eFigure 1 in Supplement). In the age subgroup analysis, we observed a continuous decline in BCS use over the years, with a more substantial decline in younger age groups and a smaller decline in older age groups. In stage I patients, the proportion of BCS on the other side decreased from 99.28 to 79.77% ($P<0.001$), accompanied by increased utilization rates of M (0.78–13.86%, $P<0.001$) and BR (0–6.4%, $P<0.001$). A similar trend was observed in stage II and III patients (eFigure 2 in Supplement). However, a slight decline in lower stages and a greater decline in higher stages. In the T-stage subgroup analysis, the proportion of BCS on the other side decreased from 99.39 to 81.01% in stage T1 patients, while the utilization rates of M (0.61–13.22%) and BR (0–5.77%) increased. A similar trend was observed in stage T2 and T3 patients (eFigure 3 in Supplement). However, a slight decline in lower T-stages and greater decline in higher T-stages were observed. The BCS rate was decreased in all races, histology and grade (eFigs. 4, 5 and 6 in Supplement).

Predictors of BCS over MBBC

Multivariate logistic regression analysis (Table 2) showed that BCS was positively correlated with older age (age ≥ 65 years: OR 2.469; 95%CI 2.040–2.988; $P<0.001$, age = 50–64 years: OR 1.256; 95%CI 1.040–1.517; $P<0.001$), and were negatively associated with recent diagnosis, late T-stage, lymph node metastasis, invasive lobular carcinoma(ILC) and chemotherapy (2005–2009: OR 0.317; 95%CI 0.248–0.404; $P<0.001$; 2010–2014: OR 0.190; 95%CI 0.150–0.240; $P<0.001$, 2015–2019: OR 0.205; 95%CI 0.162–0.259; $P<0.001$, T3: OR 0.056; 95%CI 0.031–0.101; $P<0.001$, lymph node status: OR 0.454; 95%CI 0.391–0.527; $P<0.001$, ILC: OR 0.700; 95%CI 0.584–0.838; $P<0.001$, chemotherapy: OR 0.653; 95%CI 0.563–0.758; $P<0.001$). BCS had no significant correlation with ER status, PR status, marital status, race and grade.

Impact of BCS on survival rates

The median survival time could not be determined since BCSS outcomes were available for less than 50% of the patients in the dataset. Given that BR was performed on the basis of M, the data of the BR group were merged into the M group for subsequent statistical analysis. Thus, BR and M groups were collectively referred to as the M group. Both OS and BCSS were compared in 9571 patients who underwent either BCS or M. The median survival time for all patients was 215 months (95%CI 206–227), and the median BCSS time was not reached. For all patients, the 5-year cumulative survival rate for OS was 85.7%, and the 10-year cumulative survival rate was 71.0%. The BCSS for all patients had a 5-year cumulative survival rate of 92.7% and a 10-year cumulative survival rate of 86.2%. Specifically, in the M group, the 5- and 10-year OS rates were 81.1% and 64.6%, while in the BCS group, these rates were 87.2% and 72.7%. The 5- and 10-year BCSS rates were 87.2% and 78.8% in the M group, while 94.5% and 88.4% in the BCS group, respectively. Kaplan-Meier survival analysis indicated that BCS patients had better OS ($P<0.001$) and BCSS ($P<0.001$) compared with patients receiving M (Fig. 3). Univariate Cox analysis indicated that BCS showed significant statistical differences in both OS and BCSS. Specifically, the hazard ratio (HR) for OS and BCSS were 0.717 (95% CI 0.649–0.791, $P<0.001$) and 0.484 (95% CI 0.422–0.556, $P<0.001$), respectively. Multivariate COX analysis showed that BCS was not an independent favorable prognostic factor for OS (HR = 1.012, 95% CI 0.904–1.132, $P>0.05$), indicating that the difference in OS between the BCS and M groups was not significant. Nevertheless, our findings confirmed that BCS was an independent

Table 1 Baseline characteristics of the study population

	No. (%)			
	Total (*n* = 9571)	**BCS (*n* = 7259)**	**M (*n* = 1544)**	**BR (*n* = 768)**
Year of diagnosis				
2000–2004	1401 (14.64)	1272 (17.52)	100 (6.48)	29 (3.78)
2005–2009	1980 (20.69)	1530 (21.08)	326 (21.11)	124 (16.15)
2010–2014	2654 (27.73)	1839 (25.33)	513 (33.23)	302 (39.32)
2015–2019	3536 (36.94)	2618 (36.07)	605 (39.18)	313 (40.76)
Age, years				
< 50	1111 (11.61)	750 (10.33)	165 (10.69)	196 (25.52)
50–64	3114 (32.54)	2229 (30.71)	480 (31.09)	405 (52.73)
≥ 65	5346 (55.86)	4280 (58.96)	899 (58.23)	167 (21.74)
Stage				
Stage 0	170 (1.78)	110 (1.52)	33 (2.14)	27 (3.52)
Stage I	6643 (69.41)	5403 (74.43)	772 (50.00)	468 (60.94)
Stage II	2263 (23.64)	1542 (21.24)	505 (32.71)	216 (28.12)
Stage III	495 (5.17)	204 (2.81)	234 (15.16)	57 (7.42)
Grade				
I/II	6331 (66.15)	5006 (68.96)	893 (57.84)	432 (56.25)
III/IV	2650 (27.69)	1828 (25.18)	546 (35.36)	276 (35.94)
Unknown	590 (6.16)	425 (5.85)	105 (6.80)	60 (7.81)
T stage				
T0	150 (1.57)	100 (1.38)	29 (1.88)	21 (2.73)
T1	7414 (77.46)	5955 (82.04)	928 (60.10)	531 (69.14)
T2	1766 (18.45)	1153 (15.88)	434 (28.11)	179 (23.31)
T3	241 (2.52)	51 (0.70)	153 (9.91)	37 (4.82)
Lymph_node_status				
Negative	7753 (81.01)	6117 (84.27)	1023 (66.26)	613 (79.82)
Positive	1817 (18.98)	1141 (15.72)	521 (33.74)	155 (20.18)
Unknown	1 (0.01)	1 (0.01)	0 (0.00)	0 (0.00)
ER_Status				
Negative	1873 (19.57)	1286 (17.72)	372 (24.09)	215 (27.99)
Positive	7274 (76.00)	5663 (78.01)	1089 (70.53)	522 (67.97)
Unknown	424 (4.43)	310 (4.27)	83 (5.38)	31 (4.04)
PR_Status				
Negative	3126 (32.66)	2215 (30.51)	596 (38.60)	315 (41.02)
Positive	5943 (62.09)	4673 (64.38)	853 (55.25)	417 (54.30)
Unknown	502 (5.25)	371 (5.11)	95 (6.15)	36 (4.69)
HER2 status				
Negative	5179 (54.11)	3807 (52.45)	875 (56.67)	497 (64.71)
Positive	662 (6.92)	420 (5.79)	167 (10.82)	75 (9.77)
Unknown	3730 (38.97)	3032 (41.77)	502 (32.51)	196 (25.52)
Radiotherapy				
NO/Unknown	4285 (44.77)	2354 (32.43)	1260 (81.61)	671 (87.37)
YES	5286 (55.23)	4905 (67.57)	284 (18.39)	97 (12.63)
Chemotherapy				
NO/Unknown	6866 (71.74)	5436 (74.89)	994 (64.38)	436 (56.77)
YES	2705 (28.26)	1823 (25.11)	550 (35.62)	332 (43.23)
Histology				
IDC	7678 (80.22)	5883 (81.04)	1178 (76.30)	617 (80.34)
ILC	1058 (11.05)	743 (10.24)	228 (14.77)	87 (11.33)
Other	835 (8.72)	633 (8.72)	138 (8.94)	64 (8.33)
Marital status				
Married	5120 (53.49)	3879 (53.44)	749 (48.51)	492 (64.06)
Unmarried	3979 (41.57)	3030 (41.74)	705 (45.66)	244 (31.77)

Table 1 (continued)

	No. (%)			
	Total (*n* = 9571)	**BCS (*n* = 7259)**	**M (*n* = 1544)**	**BR (*n* = 768)**
Unknown	472 (4.93)	350 (4.82)	90 (5.83)	32 (4.17)
Race				
Black	970 (10.13)	703 (9.68)	185 (11.98)	82 (10.68)
White	7873 (82.26)	6015 (82.86)	1226 (79.40)	632 (82.29)
Other	728 (7.61)	541 (7.45)	133 (8.61)	54 (7.03)

Abbreviations: BCS breast-conserving surgery, M mastectomy, BR breast-reconstruction, ER estrogen receptor, PR progesterone receptor, HER2 human epidermal growth factor 2, IDC invasive ductal carcinoma, ILC invasive lobular carcinoma

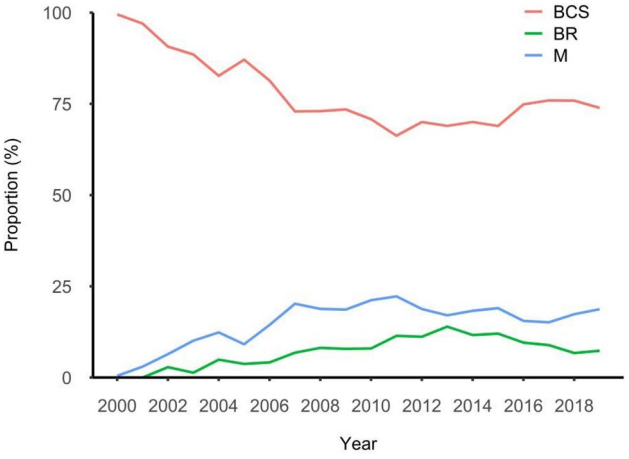

Fig. 2 Trends in unilateral breast-conserving surgery with contralateral different breast surgery in patients with MBBC from 2000 to 2019. (BCS: $P < 0.001$; M: $P < 0.001$; BR: $P < 0.001$). *BCS, breast-conserving surgery; M, mastectomy; BR, breast-reconstruction*

favorable prognostic factor for BCSS (HR = 0.746, 95% CI 0.634, 0.877; $P < 0.05$) (Tables 3 and 4).

Further subgroup comparisons revealed that BCS had significant effects on OS and BCSS in all three age groups (age < 50years: OS: $P = 0.002$; BCSS: $P = 0.002$;age 50–64 years: OS: $P < 0.05$; BCSS: $P < 0.001$; age > 65 years: OS: $P < 0.001$; BCSS: $p < 0.001$; eFigure 7 in Supplement). BCS had a significant effect on OS and BCSS in stage II patients (OS: $P < 0.001$; BCSS: $P < 0.001$), but there was no significant effect on OS and BCSS in patients with stage 0, I and III (eFigure 8 in Supplement). In the stage T0-3 group, BCS had significant effect on OS and BCSS in stage T2 and T3 patients (T2: OS: $P < 0.001$; BCSS: $P < 0.001$; T3: OS: $P = 0.005$; BCSS: $P = 0.003$). And it had significant effect on OS ($P = 0.044$) and BCSS ($P < 0.001$) in stage T1 patients. But it had no significant effect on OS and BCSS in stage T0 patients (OS: $P = 0.850$, BCSS: $P = 0.998$; eFigure 9 in Supplement). In addition, BCS had significant effects on OS and BCSS in subgroups of patients with race (white and black), histology (IDC and ILC), and grade (grade I/II, grade III/IV)(eFigures 10, 11, and 12 in Supplement).

Discussion

In MBBC, there are few reports on the survival benefits of bilateral BCS. To the best of our knowledge, our study is the first to analyze survival outcomes associated with bilateral BCS in patients with stage T0-T3 and stage 0-III MBBC using a large population database, providing insight into the role of BCS in the treatment of MBBC. Our research revealed that a significant number of patients with MBBC opted to retain both breasts. The decision to undergo BCS for contralateral breast cancer is frequently influenced by various factors, including an early onset of the contralateral disease, small tumor size, older age at the time of diagnosis, as well as considerations such as reduced trauma, quicker healing, and minimal impact on breast appearance and overall quality of life. Pyfer et al. [20] analyzed data from 11,645 breast cancer patients in the National Surgical Quality Improvement Program (NSQIP) database to compare the ages of those who opted for BCS versus BR. Their analysis revealed that the average age in the BCS group was significantly higher (61.7 vs. 53.5 years, $P < 0.01$). Similarly, Kummerow et al. [21] using data from the SEER-Medicare database, found that older breast cancer patients were more likely to choose BCS. Their study observed a decrease in the proportion of patients opting for mastectomy and reconstruction with increasing age. These findings align with our results and may be attributable to the overall health conditions of older patients, their increased sensitivity to surgical risks, and the typically lower malignancy of their tumors [22].

However, during the study, we also found that from 2000 to 2019, the use rate of BCS on one side of MBBC and BCS on the other side gradually decreased, while the usage rate of M and BR gradually increased. This result was also confirmed in the age subgroup, where the use of BCS decreased from year to year, and the change was more pronounced in the younger age groups, but the decline was smaller in older age groups. Indeed, this change is inseparable from the improvement of the BR rate after breast cancer surgery. In the United States, the BR rate after breast cancer surgery increased from 8% in 1995 to 41% in 2013 [23]. However, a decrease in contralateral BCS rate may also be related to patients'

Table 2 Multivariate model of factors predicting BCS among MBBC patients

	OR	95%CI	*P*
Year of diagnosis			
2000–2004	Ref		
2005–2009	0.317	0.248, 0.404	< 0.001
2010–2014	0.190	0.150, 0.240	< 0.001
2015–2019	0.205	0.162, 0.259	< 0.001
Age, years			
< 50			
50–64	1.256	1.040, 1.517	0.018
≥ 65	2.469	2.040, 2.988	< 0.001
Grade			
I/II			
III/IV	0.927	0.801, 1.073	0.313
Unknown	0.990	0.781, 1.256	0.935
T stage			
T0			
T1	1.276	0.810, 2.010	0.293
T2	0.751	0.470, 1.202	0.233
T3	0.056	0.031, 0.101	< 0.001
Lymph_node_status			
Negative			
Positive	0.454	0.391, 0.527	< 0.001
ER_Status			
Negative			
Positive	1.087	0.898, 1.316	0.393
Unknown	0.941	0.502, 1.762	0.849
PR_Status			
Negative			
Positive	1.082	0.923, 1.269	0.329
Unknown	0.968	0.544, 1.722	0.911
Radiotherapy			
NO/Unknown			
YES	14.835	12.875, 17.094	< 0.001
Chemotherapy			
NO/Unknown			
YES	0.653	0.563, 0.758	< 0.001
Histology			
IDC			
ILC	0.700	0.584, 0.838	< 0.001
Other	0.922	0.735, 1.158	0.486
Marital_status			
Married			
Unmarried	1.014	0.900, 1.144	0.816
Unknown	1.164	0.902, 1.502	0.244
Race			
Black			
White	0.863	0.715, 1.042	0.127
Other	0.864	0.660, 1.132	0.289

Abbreviations: BCS breast-conserving surgery, M mastectomy, BR breast-reconstruction, ER estrogen receptor, PR progesterone receptor, HER2 human epidermal growth factor 2, IDC invasive ductal carcinoma, ILC invasive lobular carcinoma

concern about postoperative radiotherapy for BCS. We considered whether the reason for the decline in contralateral BCS rate might be related to patients' concern about postoperative radiotherapy for BCS. Clinical trials by Taylor et al. [24] have identified that breast radiotherapy can lead to the development of secondary cancers and ischemic heart disease. A meta-analysis further revealed that ionizing radiation exposure to the heart during breast cancer radiotherapy increases the risk of coronary heart disease and cardiac mortality [25]. Marinelli et al. [26] analyzed long-term health data of breast cancer patients who underwent radiotherapy and found a significantly elevated risk of secondary cancers, particularly among younger women. Gupta et al. [27] investigated the persistence of this risk despite advancements in radiotherapy technology, and found that it remained particularly pronounced in patients receiving left-sided breast radiotherapy. Therefore, patients' concerns about these risks are warranted. Additionally, these risks might be influenced by factors such as accessibility and the economic burden of radiation therapy.

As we all know, most women with early stage breast cancer prefer BCS. Breast radiation therapy is usually performed after BCS to reduce the risk of local recurrence and thus avoid M. Randomized trials have shown that radiation therapy for early stage breast cancer reduces the rate of breast cancer recurrence and mortality [28]. A recent study found that the OS and BCSS of Korean early breast cancer patients receiving BCS with radiotherapy were better or at least not inferior to the M group after comparing the population in KBCR and AMC databases [29]. This indicates that radiotherapy after BCS is safe and feasible in the treatment of UBC. In the special population of MBBC, bilateral BCS means that patients may have to receive two radiotherapy treatments, which may increase the risk of heart disease and increase the incidence of radiation-related tumors. However, according to our findings, radiotherapy is an independent prognostic factor for OS and BCSS in MBBC patients. Therefore, we found that radiotherapy does not adversely affect the prognosis of MBBC patients. This is consistent with the results of BCS combined with radiation therapy for UBC.

Moreover, our Univariate Cox analysis indicated that BCS showed significant statistical differences in both OS and BCSS. In multivariate COX analysis, BCS was not identified as an independent prognostic factor for OS, but it was an independent prognostic factor for BCSS. Subgroup analyses further confirmed these results, with consistent survival outcomes observed across all age groups, tumor stage, and T-stage. Therefore, bilateral BCS is safe in the MBBC population. This is consistent with the prognostic outcomes of BCS for UBC. Previous studies have shown that BCS treatment for unilateral

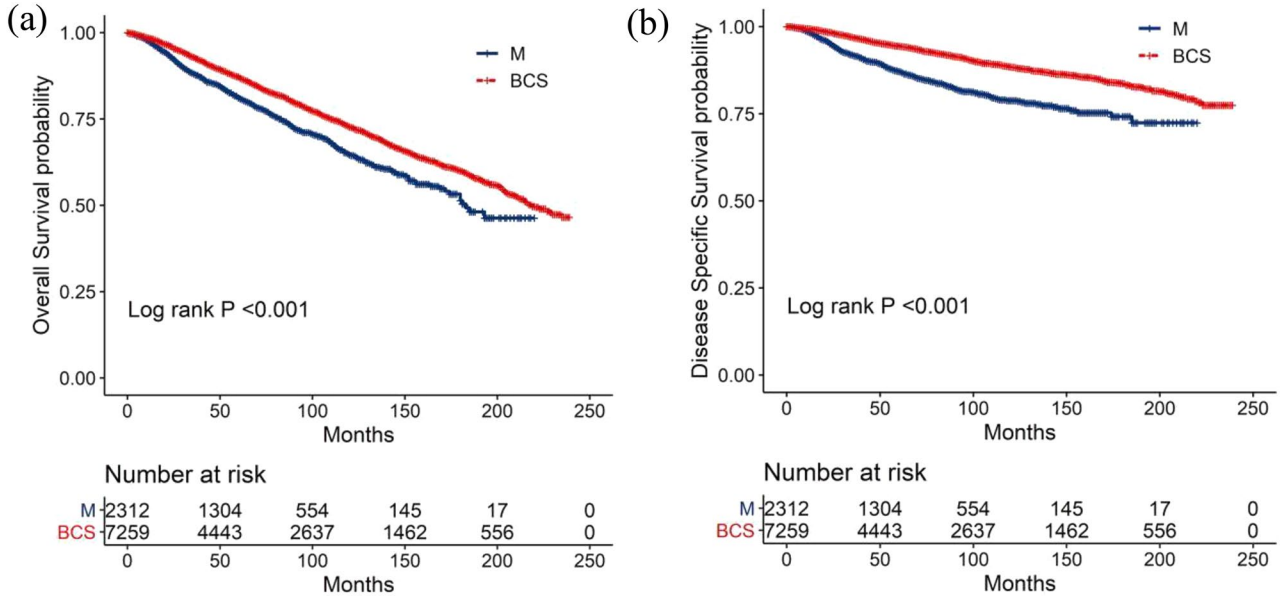

Fig. 3 Kaplan–Meier survival curves for the effects of surgery types on OS (**a**) and BCSS (**b**). *BCS, breast-conserving surgery; M, mastectomy; BR, breast-reconstruction*

early breast cancer can achieve the same long-term survival effect as M, with less surgical trauma and higher aesthetic appearance [30]. In 2020, a study in the United States carried out a matching analysis of the survival status of more than 100,000 early breast cancer patients in the past 10 years. The results showed that the 5-year OS rate of BCS treatment patients was significantly higher than that of M patients (92.9% vs.89.7%, $P < 0.001$) [31]. A study by the Danish Breast Cancer Collaborative Group found that patients assigned to BCS had better survival rates than those assigned to M [32].

Considering the better survival outcomes for breast cancer patients over the past few decades [33], the quality of life of patients after surgery is also becoming increasingly important. Compared to M, BCS offers better aesthetic results and advantages in terms of postoperative body image [34, 35]. A recent meta-analysis showed that BCS leads to better outcomes in terms of body image, future prospects, and fewer systemic side effects [36]. Moreover, for young women, the lack of breasts after M will greatly affect the patient's self-esteem, affect the future marriage relationship, breastfeeding, etc., so that patients are prone to anxiety, depression, low self-esteem and other negative emotions, affecting the treatment effect [37]. BCS can effectively solve this problem without affecting the treatment effect, and improve the aesthetics of BC treatment [38]. Although the incidence of BR after M is constantly increasing, Pyfer et al. [20] analyzed the early postoperative results of 11,645 breast cancer patients, and found that the probability of total complications, poor wound healing, infection and bleeding in the BCS group was significantly lower than that in the implant reconstruction group after M. Flanagan et al. [39] retrospectively analyzed 3233 patients with early breast cancer who underwent BCS or BR, and found that the breast satisfaction and quality of life scores of patients in the BCS group were significantly higher than those in the BR group after M. In this study, bilateral BCS treatment for MBBC is considered safe and feasible. After full communication between the clinician and the patient, if BCS has been performed on one side, when breast cancer is found on the other side, if it is eligible for BCS, BCS can be considered on the other side to avoid unnecessary extensive surgery. BCS is an independent prognostic factor affecting patients' BCSS and can also improve the aesthetics of patients and reduce postoperative complications, so more BCS can be advocated under appropriate conditions.

However, this study has several limitations. Notably, current research indicates that bilateral breast cancer occurrence is associated with BRCA1/BRCA2 mutations. For BRCA1 mutation carriers, the risk of developing contralateral breast cancer within 10 years of the initial diagnosis is approximately 20–30%, while for BRCA2 mutation carriers, the 10-year incidence is around 15–20%, both significantly higher than in the general population [40]. Unfortunately, the SEER database lacks critical genetic information, such as BRCA mutation status, which limits our ability to fully account for the risk in patients with bilateral breast cancer and may impact the assessment of their long-term prognosis. Additionally, this study lacks detailed information on several factors, including HER2 receptor expression data from before 2010, sociodemographic data, family history, internal

Table 3 Univariate and multivariate Cox regression model analyses of prognostic factors of OS

	Univariate analysis	*p*	Multivariate analysis	*p*
	HR (95%CI)		HR (95%CI)	
Surgery type				
M (or BR)	1 [Reference]		1 [Reference]	
BCS	0.717 (0.649, 0.791)	< 0.001	1.012 (0.904, 1.132)	0.834
Year of diagnosis				
2000–2004	1 [Reference]			
2005–2009	1.694 (1.500, 1.912)	< 0.001	1.391 (1.228, 1.576)	< 0.001
2010–2014	1.987 (1.736, 2.273)	< 0.001	1.501 (1.303, 1.729)	< 0.001
2015–2019	1.731 (1.445, 2.074)	< 0.001	1.259 (1.045, 1.517)	0.015
Age, years				
< 50	1 [Reference]			
50–64	1.049 (0.893, 1.233)	0.557	1.139 (0.966, 1.342)	0.121
≥ 65	3.072 (2.656, 3.553)	< 0.001	3.074 (2.629, 3.593)	< 0.001
Grade				
I/II	1 [Reference]			
III/IV	1.160 (1.060, 1.270)	0.001	1.257 (1.130, 1.399)	< 0.001
Unknown	1.029 (0.861, 1.231)	0.75	1.012 (0.838, 1.222)	0.901
T stage				
T0	1 [Reference]			
T1	1.593 (1.064, 2.384)	0.024	1.899 (1.225, 2.944)	0.004
T2	2.503 (1.663, 3.768)	< 0.001	2.927 (1.871, 4.577)	< 0.001
T3	5.156 (3.280, 8.106)	< 0.001	5.678 (3.478, 9.271)	< 0.001
Lymph_node_status				
Negative	1 [Reference]			
Positive	1.579 (1.435, 1.738)	< 0.001	1.641 (1.475, 1.826)	< 0.001
ER_Status				
Negative	1 [Reference]			
Positive	0.921 (0.832, 1.020)	0.113	0.953 (0.826, 1.100)	0.513
Unknown	0.891 (0.742, 1.071)	0.221	1.304 (0.868, 1.959)	0.201
PR_Status				
Negative	1 [Reference]			
Positive	0.849 (0.776, 0.928)	< 0.001	0.859 (0.763, 0.966)	0.012
Unknown	0.807 (0.684, 0.953)	0.011	0.682 (0.469, 0.991)	0.045
Radiotherapy				
NO/Unknown	1 [Reference]			
YES	0.616 (0.566, 0.670)	< 0.001	0.685 (0.624, 0.752)	< 0.001
Chemotherapy				
NO/Unknown	1 [Reference]			
YES	0.741 (0.674, 0.816)	< 0.001	0.695 (0.620, 0.780)	< 0.001
Histology				
IDC	1 [Reference]			
ILC	1.198 (1.046, 1.373)	0.009	0.952 (0.825, 1.099)	0.504
Other	1.103 (0.962, 1.265)	0.162	1.122 (0.968, 1.299)	0.126
Marital_status				
Married	1 [Reference]			
Unmarried	1.757 (1.612, 1.914)	< 0.001	1.522 (1.394, 1.661)	< 0.001
Unknown	1.323 (1.069, 1.637)	0.01	1.072 (0.864, 1.329)	0.528
Race				
Black	1 [Reference]			
White	0.976 (0.853, 1.116)	0.718	0.957 (0.833, 1.100)	0.536
Other	0.637 (0.507, 0.800)	< 0.001	0.707 (0.561, 0.890)	0.003

Abbreviations: OS overall survival, HR hazard ratio, CI confidence interval, BCS breast-conserving surgery, M mastectomy, BR breast-reconstruction, ER estrogen receptor, PR progesterone receptor, HER2 human epidermal growth factor 2, IDC invasive ductal carcinoma, ILC invasive lobular carcinoma

Table 4 Univariate and multivariate Cox regression model analyses of prognostic factors of BCSS

	Univariate analysis	***p***	**Multivariate analysis**	***p***
	HR (95%CI)		**HR (95%CI)**	
Surgery type				
M (or BR)	1 [Reference]		1 [Reference]	
BCS	0.484 (0.422, 0.556)	**< 0.001**	0.746 (0.634, 0.877)	< 0.001
Year of diagnosis				
2000–2004	1 [Reference]			
2005–2009	1.462 (1.217, 1.755)	**< 0.001**	1.266 (1.048, 1.530)	0.015
2010–2014	1.525 (1.254, 1.854)	**< 0.001**	1.306 (1.059, 1.610)	0.012
2015–2019	1.030 (0.785, 1.352)	0.832	0.939 (0.707, 1.246)	0.662
Age, years				
< 50	1 [Reference]			
50–64	0.715 (0.594, 0.860)	**< 0.001**	0.856 (0.708, 1.035)	0.109
≥ 65	0.927 (0.778, 1.104)	0.397	1.221 (1.005, 1.483)	0.045
Grade				
I/II	1 [Reference]			
III/IV	2.101 (1.839, 2.400)	**< 0.001**	1.517 (1.294, 1.778)	< 0.001
Unknown	1.530 (1.175, 1.992)	**0.002**	1.365 (1.032, 1.806)	0.029
Tstage				
T0	1 [Reference]			
T1	1.254 (0.690, 2.278)	0.458	1.397 (0.729, 2.675)	0.313
T2	3.095 (1.696, 5.649)	**< 0.001**	2.412 (1.246, 4.671)	0.009
T3	7.259 (3.814, 13.816)	**< 0.001**	4.915 (2.431, 9.935)	< 0.001
Lymph_node_status				
Negative	1 [Reference]			
Positive	2.911 (2.552, 3.322)	**< 0.001**	2.329 (2.009, 2.701)	< 0.001
ER_Status				
Negative	1 [Reference]			
Positive	0.557 (0.483, 0.641)	**< 0.001**	0.953 (0.779, 1.166)	0.642
Unknown	0.671 (0.512, 0.880)	**0.004**	1.561 (0.843, 2.892)	0.157
PR_Status				
Negative	1 [Reference]			
Positive	0.549 (0.480, 0.627)	**< 0.001**	0.717 (0.598, 0.859)	< 0.001
Unknown	0.650 (0.505, 0.838)	**0.001**	0.570 (0.318, 1.022)	0.059
Radiotherapy				
NO/Unknown	1 [Reference]			
YES	0.640 (0.562, 0.728)	**< 0.001**	0.801 (0.692, 0.926)	0.003
Chemotherapy				
NO/Unknown	1 [Reference]			
YES	1.493 (1.310, 1.703)	**< 0.001**	0.792 (0.675, 0.930)	0.005
Histology				
IDC	1 [Reference]			
ILC	1.061 (0.855, 1.316)	0.591	0.942 (0.748, 1.186)	0.611
Other	0.923 (0.737, 1.157)	0.487	1.002 (0.785, 1.281)	0.985
Marital_status				
Married	1 [Reference]			
Unmarried	1.388 (1.217, 1.583)	**< 0.001**	1.305 (1.140, 1.493)	< 0.001
Unknown	1.057 (0.756, 1.477)	0.748	0.970 (0.691, 1.362)	0.862
Race				
Black	1 [Reference]			
White	0.609 (0.511, 0.726)	**< 0.001**	0.807 (0.671, 0.970)	0.022
Other	0.486 (0.354, 0.667)	**< 0.001**	0.639 (0.463, 0.882)	0.006

Abbreviations: BCSS, breast cancer-specific survival, HR hazard ratio, CI confidence interval, BCS breast-conserving surgery, M mastectomy, BR breast-reconstruction, ER estrogen receptor, PR progesterone receptor, HER2 human epidermal growth factor 2, IDC invasive ductal carcinoma, ILC invasive lobular carcinoma

medicine comorbidities, use of endocrine therapy, specific radiation therapy methods, doses and ranges of radiation, radiation-related tumors, and radiation-induced heart disease. These factors may also influence surgical choices and patient survival outcomes. Furthermore, as a retrospective analysis, our findings must be interpreted within the context of the available data.

Conclusions

In summary, this retrospective cohort study demonstrates that the usage rate of bilateral BCS has been declining over the past two decades in this particular population with MBBC, but we found that the patients who were old or with smaller tumor size were more likely to choose BCS for contralateral breast cancer. At the same time, our study concluded that BCS had no effect on patients' OS, but BCS was an independent prognostic factor for BCSS. However, for a more comprehensive understanding, multicenter prospective research is necessary to further determine whether BCS is still an independent prognostic factor for BCSS in MBBC.

Abbreviations

BCS	Breast-conserving surgery
MBBC	Metachronous bilateral breast cancer
M	Mastectomy
BR	Breast-reconstruction
IDC	Invasive ductal carcinoma
ILC	Invasive lobular carcinoma
SEER	Surveillance, Epidemiology, and End Results
HRs	Hazard ratios
ER	Estrogen receptor
PR	Progesterone receptor
HER2	Human-epidermal growth factor receptor 2
OS	Overall survival
BCSS	Breast cancer-specific survival
UBC	Unilateral breast cancer
BBC	Bilateral breast cancer
SBBC	Synchronous bilateral breast cancer

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-025-03685-4.

Supplementary Material 1

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Author contributions

YY was responsible for the concept and design of the study. All authors contributed to the acquisition, analysis, and interpretation of the data. The draft was produced by HQ. The statistical analysis was conducted by HQ and LQ, while YY provided administrative, technical support. All authors read and approved the final manuscript.

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Data availability

Data from the SEER program is available for public. The data supporting the conclusions of this article are available in the Surveillance Epidemiology, and End Results (SEER) database (https://seer.cancer.gov/).

Declarations

Ethics approval and consent to participate

We signed the "Surveillance, Epidemiology, and End Results Program Data-Use Agreement" in accordance with the requirement of using SEER database. Therefore, we obtained the data using permission and could download data from the SEER database. The ethics committee of our hospital carries out its work in strict accordance with the Ethical Review of Biomedical Research Involving Human Beings, ICH-GCP, GCP and relevant regulations, etc., and performs the duties of biomedical research ethics review involved in human beings. The article does not belong to the scope of the ethics committee review and does not need to be reviewed according to the current ethical standards. The data on the paper is collected from public databases and belongs to public resources.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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