Original Article

Impact of surgical types on overall survival in patients with ductal carcinoma *in situ*: an analysis based on the SEER database

Guobin Jiang[1,2], Xia Ren[1,2], Xi Shang[1,2]

[1]Thyroid and Breast Surgery Department, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, Taizhou, China; [2]Thyroid and Breast Surgery Department, Enze Hospital, Taizhou Enze Medical Center (Group), Taizhou, China

Contributions: (I) Conception and design: G Jiang; (II) Administrative support: X Shang; (III) Provision of study materials or patients: X Shang; (IV) Collection and assembly of data: X Ren; (V) Data analysis and interpretation: G Jiang, X Ren; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Xi Shang, MD. Thyroid and Breast Surgery Department, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, No. 150 Ximen Street, Linhai, Taizhou 317000, China; Thyroid and Breast Surgery Department, Enze Hospital, Taizhou Enze Medical Center (Group), No. 1, Tongyang Road, Luqiao District, Taizhou 318050, China. Email: xishangenze@163.com.

Background: Breast cancer, as one of the most common malignancies among women globally, presents a concerning incidence rate, underscoring the importance of addressing the treatment of its precursor lesion, ductal carcinoma in situ (DCIS). Treatment decisions for DCIS, involving the balance between breast-conserving surgery (BCS) and mastectomy, remain an area requiring further investigation. This study aimed to compare influence of different surgical types on overall survival (OS) of patients with DCIS and identify specific subgroups with improved OS to develop an effective survival nomogram for patients.

Methods: Patient data from the Surveillance, Epidemiology, and End Results (SEER) database for DCIS cohort from 2010 to 2020 were retrieved. Kaplan-Meier (K-M) survival curves were utilized to compare prognostic OS of patients with different surgical methods. Cox regression analysis was employed to determine prognostic factors and establish a nomogram to predict 3-, 5-, and 10-year survival rates. The model was confirmed by Concordance Index (C-index), calibration curves, and receiver operating characteristic (ROC) curves.

Results: A total of 71,675 patients with DCIS were included. Patients who underwent subcutaneous mastectomy (SM) demonstrated the best OS compared to other surgical types. Additionally, adjuvant radiotherapy or chemotherapy in combination with surgery significantly improved OS compared to surgery alone. Among DCIS patients aged ≤74 years, those who underwent SM benefited the most in terms of OS, while in the age group of 63–74 years, patients who underwent BCS had significantly higher OS than those who underwent total (simple) mastectomy (TM)/modified radical mastectomy (MRM). Multiple factors were associated with improved OS in DCIS patients, and these factors were integrated into the nomogram to establish OS predictions. The C-index, calibration curves, and ROC curves indicated that the nomogram was suitable for assessing patient prognosis.

Conclusions: This study demonstrated that SM treatment yielded the best survival rates for DCIS patients, providing important guidance for future surgical decision-making. Moreover, identifying multiple independent factors related to survival and establishing reliable survival nomograms can assist physicians in developing personalized treatment plans and prolonging patient survival.

Keywords: Ductal carcinoma in situ (DCIS); mastectomy; breast-conserving surgery (BCS); nomogram; Surveillance, Epidemiology, and End Results (SEER)

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Introduction

Breast cancer (BC) is one of the most prevalent cancers among women globally. In the United States alone, according to the 2021 cancer statistics, 281,550 women were newly diagnosed with BC, and 43,600 individuals succumbed to the disease. The incidence of BC increases with age, particularly showing a sharp rise after the age of 50 (1). Ductal carcinoma in situ (DCIS) is a precursor lesion of BC, accounting for approximately 20% of BC cases detected through mammography (2,3). DCIS is characterized by the local abnormal proliferation of malignant cells within the breast ducts without invasion beyond the basement membrane into the surrounding tissue, i.e., no invasion of adjacent mesenchyme (4). Without treatment, 10–28% of DCIS patients may progress to invasive BC (5). The treatment options for DCIS include breast tumor excision (with a goal of a 2-mL surgical margin) combined with radiotherapy or mastectomy (6). Breast tumor excision with adjuvant radiotherapy is considered a breast-conserving therapy. Traditional surgery for early BC is standard breast-conserving surgery (BCS), aimed at preserving the breast as much as possible. For women with larger tumors, it may be challenging to preserve the breast while ensuring complete tumor removal compared to breast size, which may necessitate mastectomy (7). In recent years, oncoplastic breast surgery techniques have improved cosmetic outcomes by applying principles of reconstructive surgery, preserving breast appearance while removing BC, thereby reducing psychological burdens during treatment, enhancing patient satisfaction, and improving quality of life (8,9).

One study has reported that patients who undergo mastectomy have a 10-year disease-free survival rate of as high as 98%, whereas patients who undergo BCS have a disease-free survival rate of only 81% during the same period (10). However, considering that DCIS is a precursor lesion of invasion, there is a risk of overtreatment with breast surgery for many patients with small, localized DCIS lesions (11). Relevant studies have indicated that patients treated with BCS have better prognoses than those undergoing mastectomy, possibly due to improvements in radiotherapy and systemic therapy (12-14). Radiotherapy is typically used as an adjuvant therapy to eliminate residual micro-cancer cells post-surgery, improving survival rates in early non-metastatic BC patients (15,16). Patients with estrogen receptor (ER)-positive DCIS should also undergo 5 years of endocrine therapy (tamoxifen or aromatase inhibitors) (17). However, related studies have also shown that the impact of postoperative radiotherapy on patient mortality is similar between BCS and mastectomy, but BCS increases the risk of local regional recurrence (18,19). Nash *et al.*'s 2023 publication on "The Landmark Series-Ductal Carcinoma in Situ: The Evolution of Treatment" pointed out that there is currently no evidence that tamoxifen used as adjuvant therapy or for primary prevention in patients at increased risk of BC can reduce BC mortality (20). Furthermore, the survival outcomes of patients undergoing different types of surgery are also influenced by aspects such as patients' mental health and quality of life (21). Therefore, there is still a need to explore the appropriate balance between the risks and benefits of different surgical treatments for DCIS (22). Breast surgeons require specialized training and standardized protocols for different types of breast surgeries to assist women in making better, more informed decisions regarding breast surgery.

This study aimed to comprehensively analyze the influence of multiple surgical types on overall survival (OS) of DCIS

Highlight box

Key findings

- This study found that patients with ductal carcinoma in situ (DCIS) who underwent subcutaneous mastectomy (SM) demonstrated better overall survival (OS) compared to other surgical methods. Additionally, combining surgery with radiation therapy or chemotherapy significantly improved OS for patients compared to surgery alone. Integrating factors associated with OS in DCIS patients into an OS prediction model, the established survival nomograms effectively assess patient prognosis.

What is known and what is new?

- The treatment choice for DCIS involves a balance between breast-conserving surgery (BCS) and mastectomy, which remains an area worthy of ongoing exploration.
- This study provides new evidence demonstrating that SM offers optimal survival outcomes for DCIS patients compared to other surgical methods. The study identified specific subgroups that benefit from OS improvement and established reliable survival prediction nomograms.

What is the implication, and what should change now?

- Clinical physicians should consider SM as the preferred surgical approach for DCIS patients to achieve optimal survival outcomes.
- This study underscores the importance of incorporating various prognostic factors into treatment decisions and highlights the necessity of developing personalized treatment plans based on specific patient characteristics.
- The establishment of survival nomograms aids in better predicting patient prognosis and prolongs patient survival through tailored treatment strategies.

patients by utilizing the Surveillance, Epidemiology, and End Results (SEER) database. DCIS patients were categorized based on the surgical types they underwent, and Kaplan-Meier (K-M) curves were used to compare the influence of different surgical types on the OS of the entire DCIS cohort and different age groups within the DCIS population. Additionally, Cox regression analyses were performed to explore factors influencing OS in DCIS patients and construct a reliable survival nomogram for DCIS patients. These research findings help doctors better understand the advantages and disadvantages of different treatment methods, enabling them to formulate more rational surgical plans to improve treatment outcomes and provide better survival opportunities for DCIS patients. We present this article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-23-468/rc).

Methods

Data source

Our data was obtained from the SEER database that was established in 1973, and it is maintained by the National Cancer Institute (NCI) in the United States (23). SEER is a population-based research program that collects cancer-related information, including patient demographics, cancer types, treatment details, and survival information. The database covers approximately 48.0% of the U.S. population and is widely used in clinical research, cancer epidemiology studies, and cancer survival rate analyses. More information about the SEER database can be found on the website (https://seer.cancer.gov/about/overview.html).

Patient selection

The SEER database used in this study includes patient data from 17 medical centers. We used the SEER*Stat software (version 8.4.2) to extract the dataset of DCIS patients. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Since all patient information in the SEER database has been de-identified and does not contain identifiable patient-specific information, the database information is publicly accessible, therefore, patient informed consent and institutional review board ethical approval were not required.

The following criteria were utilized to identify eligible patients: (I) diagnosed between 2010 and 2020; (II) site recode ICD-O-3/WHO 2008 code for breast (site codes C50.0-C50.9); (III) primary BC, defined as the first or only cancer diagnosis for the patient (sequence number: "1st of 2 or more primaries" or "one primary only"); (IV) T stage as Tis, N stage as N0, M stage as M0; (V) histology type as DCIS. The following patients were excluded: those with unknown marital status, unknown race, unknown laterality, unknown grade, those with only a death certificate or autopsy report as evidence, unknown tumor size, unknown lymph node examination, unknown radiotherapy and chemotherapy information, and unknown surgery type. Patient selection process for this study is illustrated in *Figure 1*.

Variable collection

In this study, we collected patient demographics, tumor indicators, treatment indicators, and survival data. The demographic information included age (≤62, 63–74, >74 years), gender (male, female), race (Black, White, Others), and marital status (married, unmarried). Tumor indicators referred to the primary site [nipple/axillary tail, inner quadrant, outer quadrant, central portion, overlapping lesion, breast, not otherwise specified (NOS)], histology [intraductal, solid type (intraductal with other types of carcinoma *in situ*, 8,523/2; intraductal carcinoma, noninfiltrating, NOS, 8,500/2; DCIS, solid type, 8,230/2), comedocarcinoma (comedocarcinoma, noninfiltrating, 8,501/2), cribriform (cribriform carcinoma *in situ*, 8,201/2), papillary (intraductal micropapillary carcinoma, 8,507/2; noninfiltrating intraductal papillary adenocarcinoma, 8,503/2; papillary carcinoma *in situ*, 8,050/2)], laterality (left, right), grade classification (I—well differentiated, II—moderately differentiated, III—poorly differentiated, IV—undifferentiated), tumor size (≤4, 5–11, >11 mm), lymph node examination (no, yes), ER status (negative, positive, borderline/unknown), progesterone receptor (PR) status (negative, positive, borderline/unknown), and human epidermal growth factor receptor 2 (HER2) status (negative, positive, borderline/unknown). Treatment indicators included surgery type [BCS, modified radical mastectomy (MRM), radical mastectomy (RM), subcutaneous mastectomy (SM), total (simple) mastectomy (TM)], chemotherapy status, and radiotherapy status. OS was defined as the time from diagnosis to death from any cause (in months).

Statistical analysis

Data analysis was conducted by R statistical software

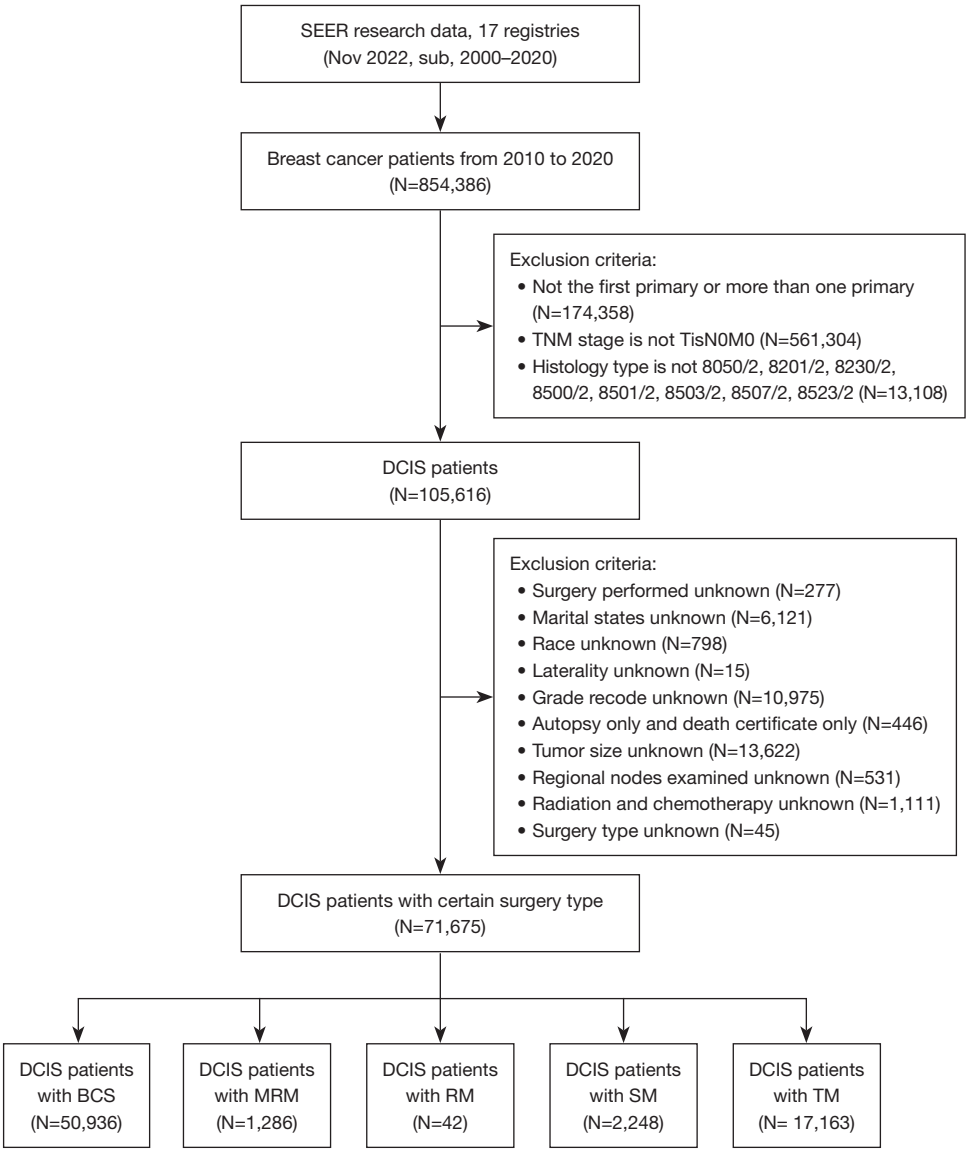

Figure 1 Sample selection flowchart. SEER, Surveillance, Epidemiology, and End Results; DCIS, ductal carcinoma in situ; BCS, breast-conserving surgery; MRM, modified radical mastectomy; RM, radical mastectomy; SM, subcutaneous mastectomy; TM, total (simple) mastectomy.

(version 4.2.3). Grouping was determined based on P values and chi-squared test values. Categorical data were shown as percentages and compared using the chi-squared test. Variables with a $P \leq 0.05$ (two-tailed) were considered to have statistically significant differences. Survival analysis was conducted by plotting survival curves using the K-M method, followed by log-rank tests to compare survival curves between different groups. Univariate Cox regression analysis was performed, and variables with a $P<0.05$ and statistical significance were subjected to the multivariate Cox analysis. Variable selection for the model was performed using the bidirectional stepwise regression method with the minimum Akaike information criterion (AIC). Hazard ratios (HRs), 95% confidence intervals (CIs), and P values were used to estimate relative risks, and the results were presented using a nomogram. The C-index was calculated to quantify the difference between observed and predicted values and assess the predictive ability of the nomogram. Receiver operating

characteristic (ROC) curves and calibration curves were plotted to validate the discriminative power and calibration of the model. X-tile software was used for optimal cutoff value analysis of age and tumor size using the K-M method (Figures S1,S2). Other statistical analyses were done on R statistical software (version 4.2.3), and the following R packages were utilized: openxlsx, rms, MASS, car, rmda, survival, survminer, foreign, and timeROC.

Results

Baseline characteristics

This study included a total of 71,675 patients diagnosed with DCIS and undergoing different types of surgery between 2010 and 2020, including BCS (50,936 cases), MRM (1,286 cases), RM (42 cases), SM (2,248 cases), and TM (17,163 cases). The demographic and clinicopathological characteristics of the five groups are listed in *Table 1*. In *Table 1*, all characteristics are statistically significant except for the laterality indicator (P=0.18). The majority of patients in this cohort were ≤62 years old (59.4%), married (63.8%), and White (74.0%). Most patients with intraductal, solid type tumor, positive ER and PR receptors, borderline/unknown HER2 status, tumors located in the upper outer quadrant, and tumor size larger than 11 mm; 61.4% of patients had no lymph node examination, 49.4% received radiotherapy, and 38.1% received chemotherapy.

Survival curve analysis

Overall, the median OS for the entire cohort was 61 months, with 3-year, 5-year, and 10-year survival probabilities of 98.4% [95% confidence interval (CI), 98.3–98.5%], 96.4% (95% CI: 96.2–96.6%), and 89.4% (95% CI: 88.9–89.8%) respectively (*Figure 2A*). In the long term, patients who underwent SM showed the greatest survival benefit (P<0.001). Patients who underwent TM had significantly higher survival benefits compared to those who underwent BCS or MRM (P<0.001 and P=0.003). However, there was no significant difference in survival benefits between patients who underwent BCS and MRM (P=0.15) (*Figure 2B*). Among all surgical approaches, BCS combined with radiotherapy had the greatest survival benefit for DCIS patients (P<0.001) (*Figure 2C*). The treatment approach of surgery combined with chemotherapy was associated with the best outcome (P<0.001), but the difference in survival impact on BCS + chemotherapy *vs.* mastectomy + chemotherapy was not significant (P=0.99) (*Figure 2D*).

Considering that age has a significant impact on the choice of surgical type and OS in DCIS patients, further evaluation was conducted to assess the influence of age and surgical type on the survival of DCIS patients. The results showed that younger DCIS patients had a significant survival advantage (P<0.001) (*Figure 3A*). Among ≤62-year-old DCIS patients, choosing SM resulted in better OS (P=0.02) (*Figure 3B*). In the 63–74-year-old DCIS patients, SM had the best survival advantage (P=0.04) (*Figure 3C*). In DCIS patients older than 74 years, the choice of surgical type did not significantly affect OS (P=0.08) (*Figure 3D*).

Factors for the OS of patients with DCIS

The results of the univariate Cox regression analysis (*Table 2*) showed that the surgery type was a significant factor for the OS of patients (P<0.001). Significant factors associated with poor OS included age greater than 62 years, unmarried status, Black, primary tumor located in the nipple/axillary tail, papillary histological type, absence of lymph node examination, tumor size larger than 11 mm, negative ER, PR, and HER2 status, no chemotherapy, and no radiotherapy (P<0.05). The multivariate Cox regression analysis further validated the independent predictive value of these factors. The results showed that the type of surgery, age, race, marital status, histological type, lymph node examinations, tumor size, PR status, and receipt of radiotherapy were independent predictors of OS in DCIS patients (*Table 2*). Significant survival disadvantages were observed in patients aged 63–74 years (HR: 3.232, 95% CI: 2.946–3.545, P<0.001) and over 74 years (HR: 9.936, 95% CI: 9.041–10.92, P<0.001). Significant survival advantages were observed in White and other races (White: HR: 0.73, 95% CI: 0.669–0.812, P<0.001; other: HR: 0.499, 95% CI: 0.429–0.58, P<0.001), patients with cribriform histological type (HR: 0.838, 95% CI: 0.737–0.952, P=0.007), patients who underwent lymph node examination (HR: 0.871, 95% CI: 0.796–0.954, P=0.003), PR-positive patients (HR: 0.873, 95% CI: 0.779–0.978, P=0.02), and patients who received radiotherapy (HR: 0.654, 95% CI: 0.601–0.711, P<0.001). Patients who were unmarried (HR: 1.563, 95% CI: 1.455–1.679, P<0.001) and patients with tumor size >11 mm (HR: 1.117, 95% CI: 1.01–1.235, P=0.03) showed poorer OS.

Table 1 Baseline characteristics of patients with DCIS

Characteristic	Total (N=71,675)	BCS (N=50,936)	MRM (N=1,286)	RM (N=42)	SM (N=2,248)	TM (N=17,163)	P value
Age							<0.001
≤62 years	42,541 (59.4)	27,951 (54.9)	862 (67.0)	31 (73.8)	1,920 (85.4)	11,777 (68.6)	
63–74 years	21,944 (30.6)	17,156 (33.7)	317 (24.7)	9 (21.4)	303 (13.5)	4,159 (24.2)	
>74 years	7,190 (10.0)	5,829 (11.4)	107 (8.3)	2 (4.8)	25 (1.1)	1,227 (7.1)	
Race							<0.001
Black	8,255 (11.5)	5,780 (11.3)	161 (12.5)	7 (16.6)	183 (8.1)	2,124 (12.4)	
White	53,043 (74.0)	38,042 (74.7)	951 (74.0)	33 (78.6)	1,658 (73.8)	12,359 (72.0)	
Other	10,377 (14.5)	7,114 (14.0)	174 (13.5)	2 (4.8)	407 (18.1)	2,680 (15.6)	
Marital status							<0.001
Married	45,712 (63.8)	32,124 (63.1)	822 (63.9)	22 (52.4)	1,620 (72.1)	11,124 (64.8)	
Unmarried	25,963 (36.2)	18,812 (36.9)	464 (36.1)	20 (47.6)	628 (27.9)	6,039 (35.2)	
Laterality							0.18
Left	36,421 (50.8)	25,963 (51.0)	616 (47.9)	19 (45.2)	1,155 (51.4)	8,668 (50.5)	
Right	35,254 (49.2)	24,973 (49.0)	670 (52.1)	23 (54.8)	1,093 (48.6)	8,495 (49.5)	
Histologic							<0.001
Intraductal, solid type	58,121 (81.2)	41,069 (80.6)	1,001 (77.8)	32 (76.2)	1,923 (85.5)	14,096 (82.1)	
Comedocarcinoma	5,764 (8.0)	3,874 (7.7)	167 (13.0)	6 (14.3)	139 (6.2)	1,578 (9.2)	
Cribriform	5,616 (7.8)	4,448 (8.7)	70 (5.5)	1 (2.4)	133 (5.9)	964 (5.6)	
Papillary	2,174 (3.0)	1,545 (3.0)	48 (3.7)	3 (7.1)	53 (2.4)	525 (3.1)	
Primary site							<0.001
Nipple/axillary tail	389 (0.5)	268 (0.5)	9 (0.7)	0	5 (0.2)	107 (0.6)	
Inner quadrant	11,873 (16.6)	8,741 (17.2)	190 (14.8)	6 (14.2)	387 (17.2)	2,549 (14.9)	
Outer quadrant	29,256 (40.8)	22,049 (43.3)	456 (35.5)	23 (54.8)	820 (36.5)	5,908 (34.4)	
Central portion	4,604 (6.4)	3,177 (6.2)	97 (7.5)	2 (4.8)	108 (4.8)	1,220 (7.1)	
Overlapping lesion	17,883 (25.0)	12,712 (25.0)	287 (22.3)	7 (16.7)	552 (24.6)	4,325 (25.2)	
Breast, NOS	7,670 (10.7)	3,989 (7.8)	247 (19.2)	4 (9.5)	376 (16.7)	3,054 (17.8)	
Grade							<0.001
I (well differentiated)	14,485 (20.2)	10,760 (21.1)	148 (11.5)	8 (19.0)	530 (23.6)	3,039 (17.7)	
II (moderately differentiated)	30,497 (42.5)	22,479 (44.2)	470 (36.5)	14 (33.3)	912 (40.5)	6,622 (38.6)	
III (poorly differentiated)	24,525 (34.3)	16,315 (32.0)	606 (47.2)	18 (42.9)	779 (34.7)	6,807 (39.7)	
IV (undifferentiated)	2,168 (3.0)	1,382 (2.7)	62 (4.8)	2 (4.8)	27 (1.2)	695 (4.0)	
Tumor size							<0.001
≤4 mm	12,468 (17.4)	10,559 (20.7)	130 (10.1)	2 (4.8)	237 (10.5)	1,540 (9.0)	
5–11 mm	21,507 (30.0)	17,274 (33.9)	279 (21.7)	7 (16.6)	436 (19.4)	3,511 (20.5)	
>11 mm	37,700 (52.6)	23,103 (45.4)	877 (68.2)	33 (78.6)	1,575 (70.1)	12,112 (70.5)	

Table 1 *(continued)*

Table 1 *(continued)*

Characteristic	Total (N=71,675)	BCS (N=50,936)	MRM (N=1,286)	RM (N=42)	SM (N=2,248)	TM (N=17,163)	P value
LN examined							<0.001
No	44,022 (61.4)	41,063 (80.6)	79 (6.1)	7 (16.7)	312 (13.9)	2,561 (14.9)	
Yes	27,653 (38.6)	9,873 (19.4)	1,207 (93.9)	35 (83.3)	1,936 (86.1)	14,602 (85.1)	
ER status							<0.001
Negative	9,118 (12.7)	5,636 (11.1)	233 (18.1)	10 (23.8)	331 (14.7)	2,908 (16.9)	
Positive	59,967 (83.7)	43,534 (85.4)	968 (75.3)	31 (73.8)	1,864 (82.9)	13,570 (79.1)	
Borderline/unknown	2,590 (3.6)	1,766 (3.5)	85 (6.6)	1 (2.4)	53 (2.4)	685 (4.0)	
PR status							<0.001
Negative	14,032 (19.6)	8,924 (17.5)	349 (27.1)	16 (38.1)	483 (21.5)	4,260 (24.8)	
Positive	47,673 (66.5)	34,918 (68.6)	799 (62.2)	25 (59.5)	1,473 (65.5)	10,458 (60.9)	
Borderline/unknown	9,970 (13.9)	7,094 (13.9)	138 (10.7)	1 (2.4)	292 (13.0)	2,445 (14.3)	
HER2							<0.001
Negative	4,294 (6.0)	3,171 (6.2)	96 (7.5)	6 (14.3)	105 (4.7)	916 (5.3)	
Positive	1,979 (2.8)	1,307 (2.6)	57 (4.4)	2 (4.7)	86 (3.8)	527 (3.1)	
Borderline/unknown	65,402 (91.2)	46,458 (91.2)	1,133 (88.1)	34 (81.0)	2,057 (91.5)	15,720 (91.6)	
Radiation							<0.001
No	36,255 (50.6)	16,064 (31.5)	1,248 (97.0)	38 (90.5)	2,161 (96.1)	16,744 (97.6)	
Yes	35,420 (49.4)	34,872 (68.5)	38 (3.0)	4 (9.5)	87 (3.9)	419 (2.4)	
Chemotherapy							<0.001
No	44,358 (61.9)	27,600 (54.2)	1,064 (82.7)	36 (85.7)	1,840 (81.9)	13,818 (80.5)	
Yes	27,317 (38.1)	23,336 (45.8)	222 (17.3)	6 (14.3)	408 (18.1)	3,345 (19.5)	

Data are shown as n (%). DCIS, ductal carcinoma in situ; BCS, breast-conserving surgery; MRM, modified radical mastectomy; RM, radical mastectomy; SM, subcutaneous mastectomy; TM, total (simple) mastectomy; NOS, not otherwise specified; LN, lymph node; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

Survival prediction nomogram and validation

A nomogram for OS was constructed using the nine independent prognostic factors selected through multivariate Cox regression analysis to predict the 3-year, 5-year, and 10-year survival rates of patients (*Figure 4A*). The concordance index (C-index) of the nomogram was 0.773, indicating a high discriminative ability and reliability of the model. Additionally, the calibration plot showed good consistency between the predicted survival rates generated by the nomogram and the observed survival rates in the actual population, as the curve closely approached the diagonal line (*Figure 4B*). The ROC curve further validated the good predictive ability of the nomogram model constructed in this study for the 3-year [area under the curve (AUC): 0.778], 5-year (AUC: 0.777), and 10-year (AUC: 0.795) survival rates (*Figure 4C*).

Discussion

In this study, patients who underwent SM had the best OS, while patients who underwent TM had significantly higher OS compared to those who underwent BCS or MRM. Furthermore, the survival advantage of surgery combined with radiotherapy or chemotherapy was significantly higher than that of surgery alone. Among DCIS patients aged ≤74 years, those who received SM had the greatest survival benefit. Additionally, among patients aged 63–74 years,

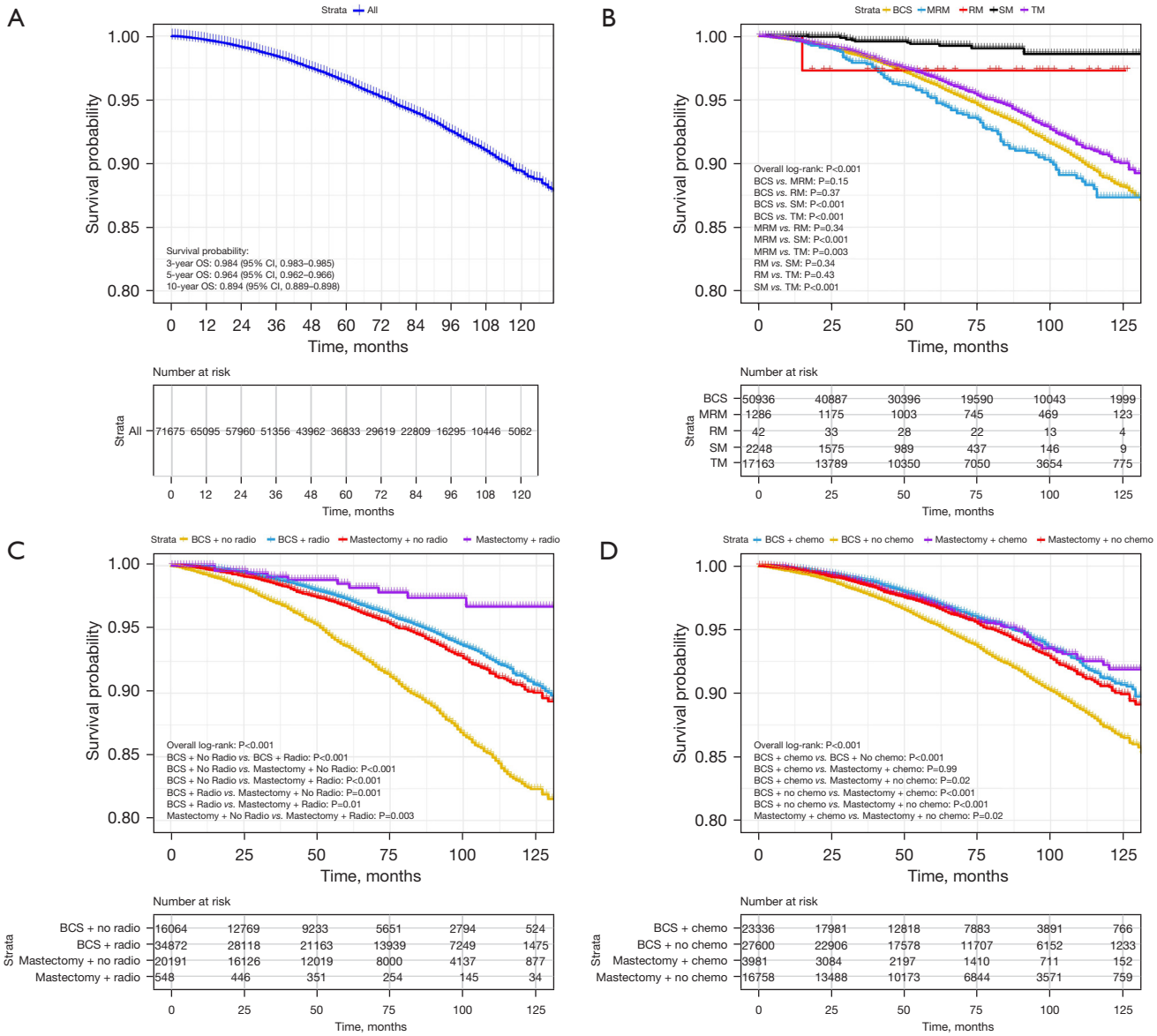

Figure 2 Survival analysis of DCIS patients. (A) OS curves of all patients; (B) survival analysis based on surgical type; (C) survival analysis based on surgery combined with radiotherapy; (D) survival analysis based on surgery combined with chemotherapy. DCIS, ductal carcinoma in situ; OS, overall survival; BCS, breast-conserving surgery; MRM, modified radical mastectomy; RM, radical mastectomy; SM, subcutaneous mastectomy; TM, total (simple) mastectomy.

BCS was associated with significantly higher OS than TM/MRM. Furthermore, significant independent prognostic factors implicated in improved OS in DCIS patients were observed, which can serve as good predictive indicators for OS in DCIS patients in clinical practice. Our findings contribute to better individualized treatment planning by doctors to improve patient survival rates and quality of life.

Before 1990, TM was considered the preferred treatment for DCIS. However, for women with small, localized DCIS, undergoing TM may be considered overtreatment as it increases the risk of complications, prolongs wound healing time, leads to scarring, and causes changes in breast shape (24). In contrast, patients who have undergone BCS are generally more satisfied with breast appearance and overall aesthetics, have higher quality of life scores, and are not significantly affected in long-term survival rates (25). A

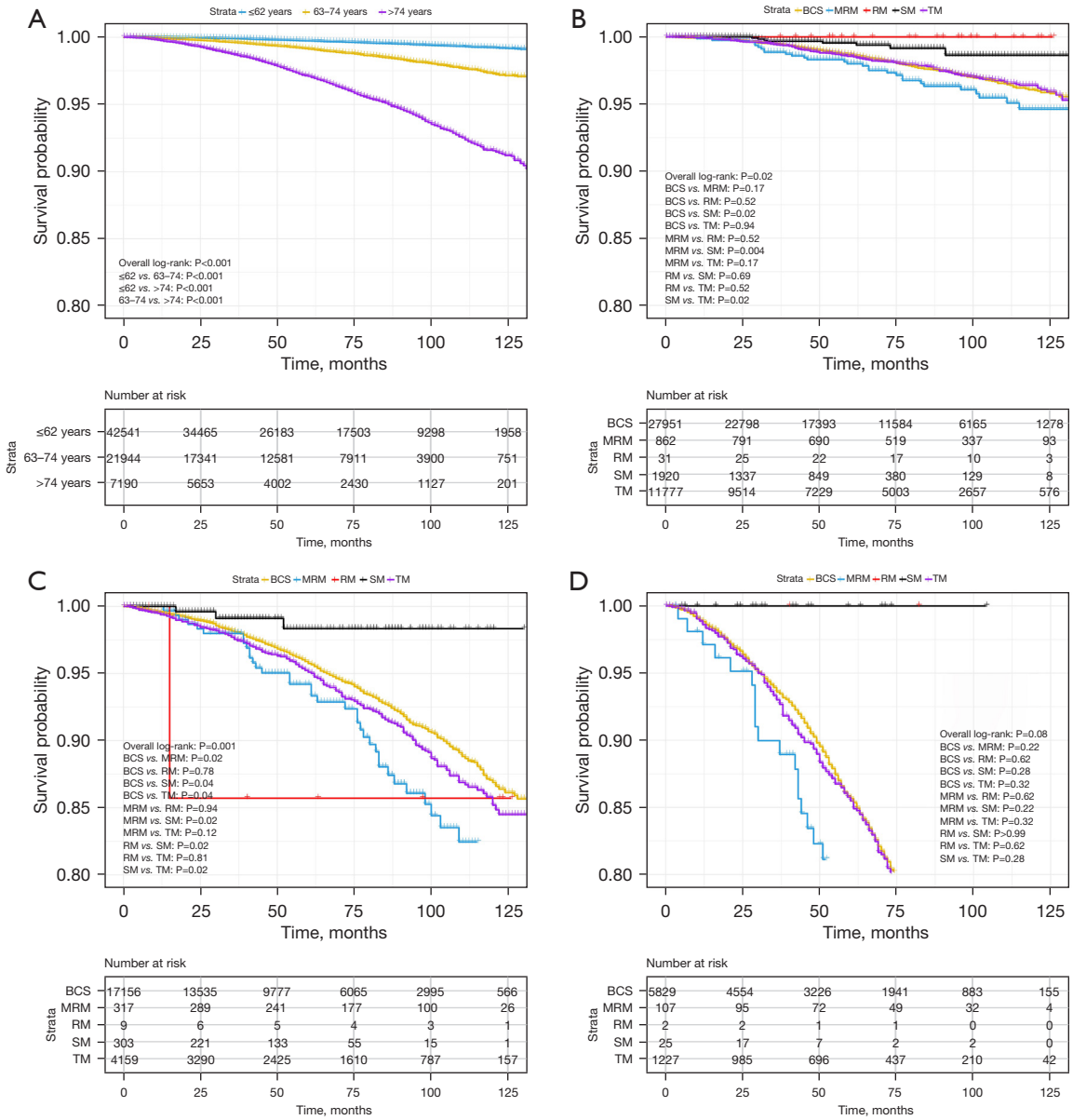

Figure 3 Age-stratified survival analysis of DCIS patients. (A) Survival analysis based on age; (B) survival analysis based on surgical type in patients ≤62 years old; (C) survival analysis based on surgical type in patients aged 63–74 years; (D) survival analysis based on surgical type in patients older than 74 years. DCIS, ductal carcinoma in situ; BCS, breast-conserving surgery; MRM, modified radical mastectomy; RM, radical mastectomy; SM, subcutaneous mastectomy; TM, total (simple) mastectomy.

recent study found that BCS + adjuvant radiotherapy had an overall recurrence rate as low as 6% at 85 months of follow-up, with margin status, multifocality, hormone receptor status, and Her-2/basal-like subtype identified as risk factors for local recurrence (26). In primary BC treatment, SM has been considered the preferred method, especially during follow-up, as SM with immediate breast reconstruction significantly reduces the risk of recurrence (27). This suggests that SM is a safe choice in treating DCIS, although longer follow-up is needed to clarify long-term risks. In a case series of DCIS patients including Brazilian cases, nipple-sparing mastectomy (NSM) has shown good tumor prognosis and a low rate of complications (28). Overall, our study further illustrates that in treating DCIS, considering

Table 2 Univariate and multivariate Cox regression analyses of OS in DCIS patients

Characteristic	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P
Surgery type				
BCS	1		1	
SM	0.155 (0.086–0.281)	<0.001	1.175 (0.948–1.458)	0.14
TM	0.857 (0.789–0.931)	<0.001	0.433 (0.061–3.084)	0.40
MRM	1.187 (0.974–1.445)	0.09	0.276 (0.152–0.502)	<0.001
RM	0.395 (0.056–2.802)	0.35	0.88 (0.787–0.984)	0.03
Age				
≤62 years	1		1	
63–74 years	3.455 (3.152–3.787)	<0.001	3.232 (2.946–3.545)	<0.001
>74 years	12.589 (11.51–13.769)	<0.001	9.936 (9.041–10.92)	<0.001
Race				
Black	1		1	
White	0.721 (0.655–0.792)	<0.001	0.737 (0.669–0.812)	<0.001
Other	0.4 (0.345–0.464)	<0.001	0.499 (0.429–0.58)	<0.001
Marital status				
Married	1		1	
Unmarried	2.329 (2.174–2.495)	<0.001	1.563 (1.455–1.679)	<0.001
Laterality				
Left	1			
Right	0.991 (0.925–1.061)	0.79		
Histologic				
Intraductal, solid type	1		1	
Comedocarcinoma	1.001 (0.895–1.12)	0.98	1.035 (0.922–1.163)	0.56
Cribriform	0.836 (0.738–0.948)	0.005	0.838 (0.737–0.952)	0.007
Papillary	1.209 (1.026–1.426)	0.02	0.982 (0.831–1.16)	0.83
Primary site				
Nipple/axillary tail	1		1	
Inner quadrant	0.671 (0.459–0.981)	0.04	0.794 (0.542–1.163)	0.24
Outer quadrant	0.695 (0.478–1.011)	0.06	0.858 (0.59–1.25)	0.43
Central portion	0.804 (0.544–1.188)	0.27	0.872 (0.589–1.29)	0.49
Overlapping lesion	0.693 (0.476–1.011)	0.06	0.803 (0.55–1.172)	0.26
Breast, NOS	0.701 (0.478–1.028)	0.07	0.83 (0.565–1.218)	0.34

Table 2 *(continued)*

Table 2 *(continued)*

Characteristic	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P
Grade				
I (well differentiated)	1		1	
II (moderately differentiated)	0.951 (0.859–1.053)	0.33	1.081 (0.975–1.199)	0.14
III (poorly differentiated)	0.864 (0.778–0.958)	0.006	1.037 (0.925–1.163)	0.54
IV (undifferentiated)	0.909 (0.759–1.087)	0.30	1.098 (0.911–1.325)	0.33
LN examined				
No	1		1	
Yes	0.782 (0.728–0.841)	<0.001	0.871 (0.796–0.954)	0.003
Tumor size				
≤4 mm	1		1	
5–11 mm	1.085 (0.978–1.204)	0.12	1.024 (0.922–1.137)	0.66
>11 mm	1.145 (1.04–1.26)	0.006	1.117 (1.01–1.235)	0.03
ER status				
Negative	1		1	
Positive	0.808 (0.733–0.89)	<0.001	0.97 (0.849–1.107)	0.65
Borderline/unknown	1.207 (1.033–1.41)	0.02	1.213 (0.978–1.505)	0.08
PR status				
Negative	1		1	
Positive	0.815 (0.75–0.885)	<0.001	0.873 (0.779–0.978)	0.02
Borderline/unknown	0.961 (0.855–1.079)	0.50	0.891 (0.758–1.046)	0.16
HER2				
Negative	1		1	
Positive	0.746 (0.597–0.932)	0.01	0.895 (0.714–1.122)	0.34
Borderline/unknown	0.856 (0.759–0.966)	0.01	0.906 (0.801–1.024)	0.11
Radiation				
No	1		1	
Yes	0.612 (0.57–0.656)	<0.001	0.654 (0.601–0.711)	<0.001
Chemotherapy				
No	1		1	
Yes	0.702 (0.65–0.758)	<0.001	0.947 (0.872–1.028)	0.20

OS, overall survival; DCIS, ductal carcinoma in situ; HR, hazard ratio; CI, confidence interval; BCS, breast-conserving surgery; SM, subcutaneous mastectomy; TM, total (simple) mastectomy; MRM, modified radical mastectomy; RM, radical mastectomy; NOS, not otherwise specified; LN, lymph node; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

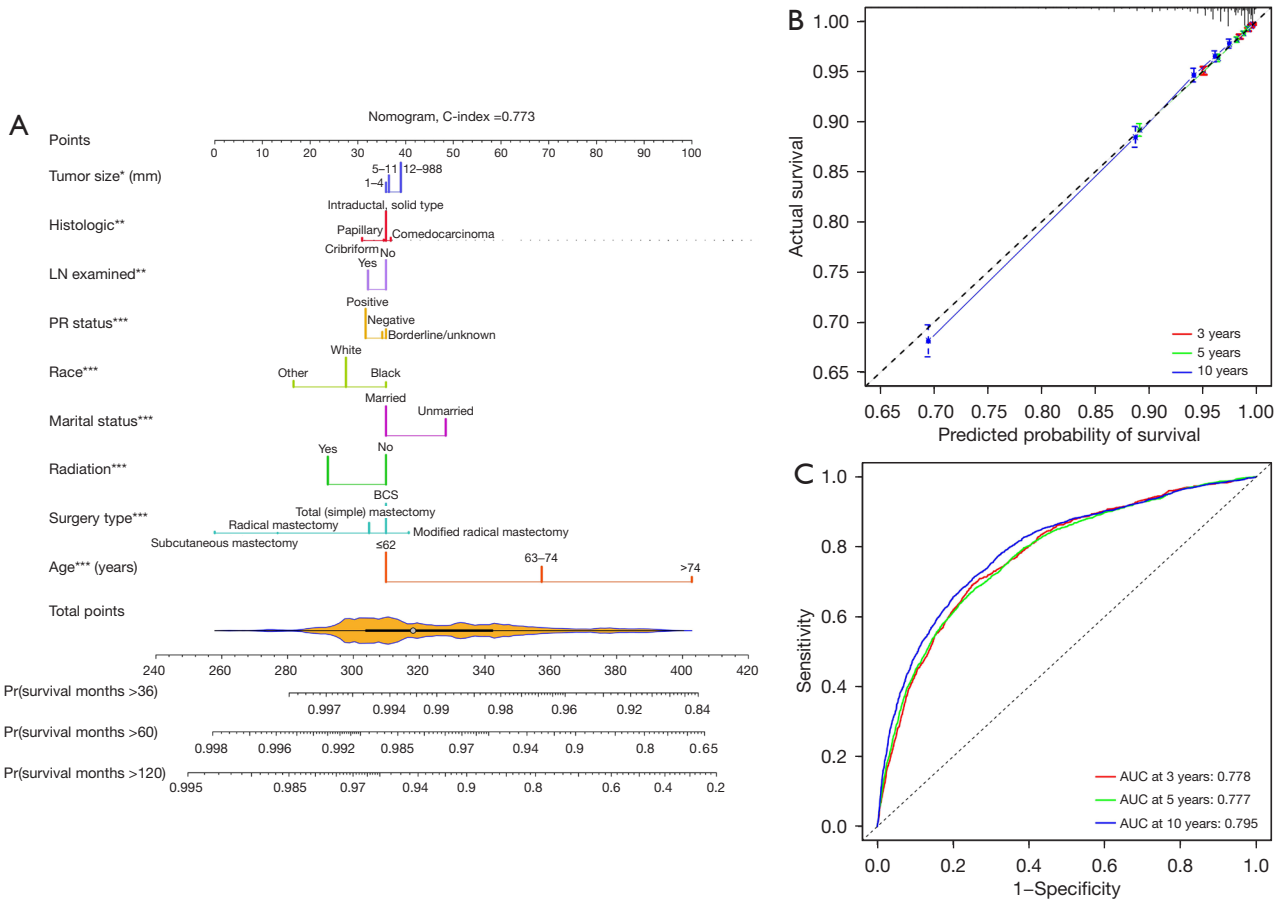

Figure 4 Nomogram and validation of OS in DCIS patients. (A) Nomogram for 3, 5, and 10 years OS; (B) calibration curves for the nomogram model at 3, 5, and 10 years; (C) ROC curves and AUC values for the nomogram model at 3, 5, and 10 years. *, P<0.05 (statistical significance); **, P<0.01 (highly statistical significance); ***, P<0.001 (extremely statistical significance). OS, overall survival; DCIS, ductal carcinoma in situ; LN, lymph node; PR, progesterone receptor; ROC, receiver operating characteristic; AUC, area under the curve.

age factors, SM still provides the greatest survival benefits among various surgical types.

In our study, radiotherapy plays a significant role in improving OS for DCIS patients, especially when combined with surgery. Multiple prospective randomized clinical trials have confirmed that whole-breast irradiation (WBI) effectively controls tumor growth at the primary site (29,30). Currently, in the United States and South Korea, the optimal treatment for DCIS is BCS, followed by WBI (31). In 2010, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) conducted a representative meta-analysis that supported these treatment trends. The study included 3,729 cases of localized excision of DCIS from four randomized controlled trials, finding that adjuvant radiotherapy reduced the incidence of ipsilateral breast events (IBE) by about half compared to non-adjuvant radiotherapy (rate ratio, 0.46). After 10 years of follow-up, radiotherapy reduced the absolute risk of any IBE by 15.2% (8). Radiation therapy remains the standard treatment for most DCIS patients undergoing breast tumor excision. Multiple studies have shown that radiotherapy is effective in treating patients, regardless of their age, extent of surgery, margin status, tamoxifen use, or clinical presentation, although it can reduce the risk of local recurrence, it does not affect OS or BC-specific survival (32-34). When complete surgical excision cannot be achieved through BCS, mastectomy is strongly recommended. It has been reported that nearly one-third of newly diagnosed DCIS patients choose this surgical treatment method (35). This surgical approach has a high local regional control rate of up to 96% and a low cancer-specific death rate of less than 4% (36). A large cohort study based on 9,938 cases

by Thompson *et al.* found that 3.2% of patients died from BC. There was no difference in overall (or BC-related) mortality rates between BCS and mastectomy (3.1% *vs.* 3.5%). Women who received adjuvant radiotherapy after BCS had a lower all-cause mortality rate (radiotherapy: 2.5% *vs.* no radiotherapy: 4.2%; P<0.001). Radiotherapy and endocrine therapy are associated with a reduced risk of further recurrence events but are not associated with BC mortality rates within 5 years of diagnosis (37). In DCIS, the prognosis is entirely based on the risk of invasive local recurrence. Studies have shown that survival rates are very low after invasive local recurrence (38-41). The data covered in this study mainly come from DCIS diagnosed in the United States SEER database between 2010 and 2020, with a more detailed grouping of surgical types and retrospective data from nearly 10 years. There is an inherent bias in the data due to the lack of detailed records on patient relapse in this study, which may be a contributing factor to the differences in OS rates studied here.

This study grouped patients by age and found that younger patients (≤62) have a higher OS rate. This could be attributed to younger women being more attentive to their health, more inclined to undergo regular breast examinations or screenings, and adopting a more proactive approach to treatment and follow-up, thus timely detecting and addressing any recurrence or progression, which improves prognosis. However, the specific prognosis of patients is closely related to the surgical approach. Byun *et al.* found that in young women with DCIS, the use of bilateral mastectomy (BM) has increased and surpassed BCS, but there is no evidence of improvement in OS (42). It has been found that young DCIS patients who undergo BCS face a higher risk of local recurrence (43). A study investigated nearly 3,000 DCIS patients who received BCS and revealed that local recurrence rate gradually decreased with increasing age. In young women, the 10-year DCIS recurrence rate was 27.3%, while in women aged 80 and above, this proportion was 7.5%. Additionally, women younger than 40 years old faced a higher risk of invasive recurrence, with 10-year invasive recurrence rates of 15.8% compared to patients aged 40 and above (6.5%) (44). Our results can be supported by these previous research conclusions, highlighting the importance of considering age factors when discussing risks and benefits of varying treatment options. Specifically, BCS had better OS than TM/MRM among patients aged 63–74 years, compared to younger patients.

Furthermore, we observed significant independent prognostic factors that were beneficial in OS of DCIS patients. Increasing evidence suggests that marital status affects survival rate of BC patients, with unmarried patients experiencing higher BC mortality rates (45,46). Early studies have shown that married patients generally have easier access to psychological and economic support, adhere to treatment plans, and benefit from early diagnosis and more appropriate treatment, leading to prolonged survival (47,48). Our results are consistent with previous research, highlighting the need for healthcare professionals to recognize that unmarried patients, especially short-term survivors, belong to a high-risk group and require more social and psychological support. These findings can prompt healthcare teams to consider patients' social support networks and psychological status when developing personalized treatment plans. For unmarried patients, providing additional psychological support, social services, and establishing support networks can improve their treatment experience and survival rates.

Our study showed that patients with favorable tumor histology such as cribriform, tumor size ≤4 mm, and lymph node examination had better OS prognosis. A comprehensive analysis demonstrated that cribriform carcinoma (CC) in BC grows slowly and invades surrounding tissues less, showing the best outcomes in OS and BC-specific survival. These findings are consistent with research based on the SEER database, further confirming the favorable histological characteristics of CC, which are implicated in improved BC-specific survival and OS (49). Typically, DCIS is considered a precursor to invasive ductal carcinoma and generally does not involve axillary lymph node metastasis. However, studies have found that approximately 4–13% of DCIS patients may have axillary lymph node metastasis (50,51). Multiple large-scale clinical studies have also confirmed that increasing tumor diameter over time is usually accompanied by an increasing risk of tumor invasion (52,53). We also found a correlation between PR status and better OS in DCIS patients. Studies have shown that in DCIS patients receiving tamoxifen treatment, the ER+/PR+ subtype has a better prognosis, and the positive hormone receptors of PR may benefit more from the cell signaling modulation effects of hormone therapy such as tamoxifen (54,55).

This study provided a profound elucidation of the potential differences in OS among DCIS patients with different surgical types and identified specific patient characteristics that would probably lead to a beneficial prognosis, further establishing a reliable survival prediction

model, which provided a robust foundation for clinical trials. However, this study has several inherent limitations. Firstly, due to the retrospective nature of the study, its results may be subject to potential biases, and further prospective trials are needed to validate the conclusions. Secondly, it is worth noting that the number of patients undergoing RM in the SEER database is limited, necessitating more research to delve deeper into the impact of this surgical type on the survival outcomes of DCIS patients. Additionally, SEER did not capture data on different postoperative local recurrence and distant metastasis rates or patients' genetic characteristics, thereby precluding further exploration at the molecular level. Finally, the data in this study only explored the overall mortality of DCIS patients, with fewer patients experiencing BC-specific mortality. Therefore, it is not possible to accurately evaluate the surgical types for DCIS-specific mortality. To validate and further deepen our research results, a larger-scale randomized controlled trial is needed, along with a more in-depth analysis of specific mortality situations, and the introduction of more dimensions of information to comprehensively study this issue.

Conclusions

This study, based on a comprehensive analysis of SEER database data, demonstrates that patients undergoing SM exhibit significantly better survival outcomes compared to other surgical methods. BCS combined with radiation therapy shows the greatest survival benefit among all surgical approaches, providing important guidance for future surgical decision-making. Age is identified as a key factor influencing treatment decisions and survival outcomes, with younger patients demonstrating notable survival advantages across various surgical types. The survival prediction nomograms developed in this study for DCIS patients assist clinicians in better formulating individualized treatment plans to extend patient survival.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-23-468/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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