

Comparison of the ductal carcinoma in situ between White Americans and Chinese Americans

Xin-Wen Kuang, MMed^a, Zhi-Hong Sun, MD^a, Jun-Long Song, MD^a, Zhanyong Zhu, MD^{b,*}, Chuang Chen, MD^{a,*}

Abstract

Currently, the wide-spread use of screening mammography has led to dramatic increases in ductal carcinoma in situ (DCIS). However, DCIS of Chinese Americans, the largest Asian subgroup in American, has rarely been comprehensively studied over the past decade. This work compared the DCIS characteristics and prognosis of Chinese American patients with White Americans in the USA to determine the characteristics and prognosis of DCIS patients of Chinese Americans.

The data were obtained using the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) data. The diagnosis and treatment variables between the two groups were compared by means of Chi-square tests. Survival was determined with the use of the Kaplan–Meier method and the multivariable Cox proportional hazard regression model.

From 1975 to 2016, 81,745 White Americans and 2069 Chinese Americans were diagnosed with ductal carcinoma in situ. Compared with the white patients, the Chinese Americans were younger (P < .001) with smaller tumors (P < .001) and higher family income (P < .001). DCIS patients of Chinese American group accounted for a higher percentage of all breast cancers than the whites (P < .001). In the multivariable Cox proportional hazard regression analysis, Chinese American was an independent favorable prognostic factor in terms of overall survival (OS) (HR, 0.684; 95% CI, 0.593–0.789; P < .001) compared with the white group.

In conclusion, DCIS characteristics of the Chinese group, which exhibited a higher proportion of younger age, a higher DCIS ratio, and a better prognosis, were distinct from those of the White Americans.

Abbreviations: BCSS = breast cancer-specific survival, BCT = breast-conserving surgery with radiation therapy, CAs = Chinese Americans, CI = confidence interval, DCIS = ductal carcinoma in situ, ER = estrogen receptor, HRs = hazard ratios, OS = overall survival, PR = progesterone receptor, SEER = surveillance, epidemiology, and end results, SPSS = Statistical Product and Service Solutions, US = United States, USA = United States of America, WAs = White Americans.

Keywords: breast cancer, breast-conserving therapy, Chinese Americans, ductal carcinoma in situ, epidemiology and end results (SEER) database, surveillance, White Americans

1. Introduction

Ductal carcinoma in situ (DCIS) is non-invasive breast cancer with a favorable prognosis.^[1–4] DCIS has become more common in the past several decades due to mammographic screening.^[5–7] In the USA, about 48,100 new DCIS cases were diagnosed in 2019, accounting for 18% of all breast cancer cases.^[8] Globally, DCIS cases also comprise nearly 20% of all detected breast cancers.^[9–12]Numerous studies have reported the demographic, clinical and pathological characteristics of DCIS in their countries.^[11,13–19] Chinese Americans (CAs) account for most

Editor: Undurti N. Das.

X-WK and Z-HS contributed equally to this work.

This work was supported by the Fundamental Research Funds for the Central Universities (grant number 2042019kf0229); the National Key Scientific Instrument and Equipment Development Project (grant number 20133655893); and the Natural Science Foundation of Hubei Province, China (grant number 2016CFB331).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the present study are available from the corresponding author on reasonable request.

The datasets generated during and/or analyzed during the present study are publicly available.

^a Department of Breast and Thyroid Surgery, ^b Department of Plastic Surgery, Renmin Hospital of Wuhan University, Wuhan, Hubei, P.R. China.

* Correspondence: Chuang Chen, Department of Breast and Thyroid Surgery (e-mail: chenc2469@163.com); Zhanyong Zhu, Department of Plastic Surgery, Renmin Hospital of Wuhan University, No 238 Jiefang Road, Wuchang District, Wuhan, Hubei 430060, P.R. China (e-mail: zyzhu@whu.edu.cn).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Received: 2 June 2020 / Received in final form: 29 October 2020 / Accepted: 8 December 2020

http://dx.doi.org/10.1097/MD.00000000024136

Ethics approval and consent to participate: The data in this research was based on the SEER database. After our signed data use agreement (https://seer.cancer.gov/ data/sample-dua.html) was approved by the SEER administration, we were allowed to access the data only for research (SEER ID: 11438 – Nov 2018). It did not contain any studies with human participants or animals performed by any of the authors. The informed consent was not required for this study.

How to cite this article: Kuang XW, Sun ZH, Song JL, Zhu Z, Chen C. Comparison of the ductal carcinoma in situ between White Americans and Chinese Americans. Medicine 2021;100:3(e24136).



of the Asian subgroups in the US.^[20] However, the current status of DCIS of Chinese Americans has rarely been comprehensively studied over the past decade. Herein, we discovered and summarized the DCIS in Chinese Americans by contrasting the features of DCIS patients in CAs versus the WAs (WAs).

2. Methods

2.1. Data collection using the SEER database

The DCIS characteristics from the USA were obtained from the latest database of the Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) [SEER*Stat Database: Incidence—SEER 9 Regs Research Data, November 2018 Sub [1975–2016] [Katrina/Rita Population Adjustment]—Linked to County Attributes—Total US, 1969–2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2019, based on the November 2018 submission). SEER*Stat (Version 8.3.5) software from SEER was used to extract the data after first obtaining permission for access to the database online (SEER ID: 11438 – Nov 2018).

The following parameters were applied for the patient selection in SEER:

- 1. breast cancer: breast (Site recode ICD-O-3/WHO 2008), female, select only the known age, cases in the research database and the first matching record for each person. The CA patients were included by selecting race/ethnicity as Chinese in the Race and Age (case data only) session.
- DCIS: breast (Site recode ICD-O-3/WHO 2008), Stage-LRD (Summary and Historic)/SEER historic stage A/In situ, 8050, 8140, 8201, 8230, 8500–8501, 8503–8504, 8507 (Site and Morphology, Histologic Type ICD-O-3 female), select only

the known age, cases in the research database and the first matching record for each person. The CA patients were included by selecting race/ethnicity as Chinese in the Race and Age (case data only) session.

3. Patients with unknown estrogen receptor (ER) and progesterone receptor (PR) status were not excluded from the analysis and patients with borderline ER or PR were defined as ERpositive or PR-positive. Only the patients enrolled after 1990 had available ER and PR status. The specific screening process was shown in Figure 1.

The selected surgery was based on the SEER research data record description APPENDIX D TWO-DIGIT SITE-SPECIFIC SUR-GERY CODES (1983-1997) (Documentation Version: April 2015) and SEER Program Coding and Staging Manual 2016. Before 1998, 10 and 20 were codes for breast-conserving surgery. After 1998, breast-conserving surgery codes including partial mastectomy, partial mastectomy with nipple resection, lumpectomy or excisional biopsy, re-excision of the biopsy site for gross or microscopic residual disease and segmental mastectomy for DCIS were 20 to 24. Mastectomy codes, including subcutaneous mastectomy, total (simple) mastectomy, modified, radical or extended radical mastectomy, were 30, 40, 50, 60, 70, 80, and 90 before 1998, and 30, 40 to 76 and 80 after 1998, respectively. Statistics of radiation therapy were obtained from SEER Radiation Therapy and Chemotherapy Information November 2018. Considering early breast cancer patients with mastectomy generally receive no radiotherapy, only patients with partial mastectomy and sequent radiation therapy and patients with mastectomy but without radiation therapy were included. In this study, breast-conserving surgery with radiation therapy (BCT) is defined as the removal of partial breast tissue with the margins of the resected surgical specimen is free of tumors with sequent radiotherapy. DCIS ratio refers to the ratio between the DCIS and all the breast cancer cases and the insurance rate is the ratio between patients with all types of insurance except Medicaid and all cases. Furthermore, Medicaid insurance includes state government-administered insurance for persons who are uninsured, below the poverty level, or covered under entitlement programs and insurance paid by a Managed Care program.

The national screening program was initiated in the mid-1980s in the USA; therefore, the patients were divided into four time intervals: 1975 to 1984, 1985 to 1994, 1995 to 2004, and 2005 to 2016.

2.2. Statistical analysis

We concluded the year of diagnosis, race, DCIS ratio, age at diagnosis, insurance status, and family income as demographic statistics. For tumor characteristics, tumor size, ER status, PR status surgery type were included. In this study, survival outcomes were overall survival (OS) and breast cancer-specific survival (BCSS). OS was defined as the time from the date of diagnosis to the date of death from any cause, or the date of the last follow-up. BCSS was calculated from the date of diagnosis to the date of death caused by breast cancer or the last clinical follow-up if death did not occur.

We compared the demographic and tumor characteristics of CAs with WAs using the Chi-square test. Unadjusted OS and

BCSS of Chinese Americans and White Americans were compared using the log-rank test and survival curves were conducted using the Kaplan–Meier method. Furthermore, the survival and prognostic factors of all cases were analyzed. Adjusted hazard ratios (HRs) with 95% confidence interval (CI) were calculated using a Cox proportional hazard regression model to estimate the survival-related factors. All statistical analyzes were performed using the SPSS 24.0 software (SPSS Inc. Chicago, IL), and a two-tailed P < .05 was considered to be statistically significant.

3. Results

3.1. Comparison of tumor characteristics of DCIS between WAs and CAs

Based on our inclusion criteria, 81,745 WAs and 2069 CAs were identified with DCIS from 1975 to 2016. The characteristics of WAs and CAs were compared and the results are shown in Table 1. The analysis indicated that the differences in the age distributions of DCIS between WAs and CAs showed statistical significance (P < .001). The median age of DCIS patients of the white remained stable from 1975 to 2016 (Fig. 2A), while that of CAs was not. The fluctuation may arise from that the number of DCIS patients of CAs in the early years was insufficient. Additionally, the mostly higher median age was observed in the WAs than CAs.

Table 1

Items	White Americans		Chinese Americans		
	Number	Ratio (%)	Number	Ratio (%)	Р
Number (DCIS ratio)	81,745	7.90	2069	10.90	<.001
Time intervals (DCIS ratio)					
1975–1984	1983	2.30	27	3.90	.005
1985–1994	8011	5.60	155	8.30	<.001
1995–2004	27,814	8.60	660	11.80	<.001
2005–2016	43,937	9.30	1227	11.30	<.001
Age distribution (years)					
<40	2924	3.60	103	5.00	<.001
40–54	29,458	36.00	967	46.70	
55–69	32,975	40.30	745	36.00	
>69	16,388	20.00	254	12.30	
Tumor size					
<4 cm	33,038	40.40	973	47.00	<.001
≧4 cm	3539	4.30	144	7.00	
Unknown	45,168	55.30	952	46.00	
Estrogen receptor (1990+)					
Positive or borderline	37,641	46.00	1004	48.50	.003
Negative	8774	10.70	247	11.90	
Unknown	35,330	43.20	818	39.50	
Progesterone receptor (1990+)					
Positive or borderline	30,723	37.60	849	41.00	.003
Negative	12,855	15.70	328	15.90	
Unknown	38,167	46.70	892	43.10	
Insurance Recode (2007+)					
Insured	33,189	40.60	921	44.50	<.001
Medicaid	2363	2.90	121	5.80	
Not insured	376	0.50	9	0.40	
Insurance status unknown	45,817	56.00	1018	49.20	
Surgery pattern					
Mastectomy without radiotherapy	33,888	41.50	900	43.50	.062
Breast-conserving therapy	47,857	58.50	1169	56.50	
Median family income (\$)					
<46,450	7573	9.30	10	0.50	<.001
46,451-56,490	21,086	25.80	361	17.40	
56,491-70,820	22,370	27.40	252	12.20	
>70,820	30,716	37.60	1446	69.90	
Median family income (mean) (\$)	6444.45		7904.55		
10-year OS		91.12		95.94	<.001
10-year BCSS		99.16		99.57	.038

BCSS = breast cancer-specific survival, CAs = Chinese Americans, OS = overall survival, WAs = White Americans.



Figure 2. (A) Comparisons of the median age of the White Americans (WAs) from 1976 to 2016 to that of the Chinese Americans (CAs). (B) Comparisons of the percentage of tumors smaller than 4 cm between the WAs and CAs from 2004 to 2016. (C) Comparisons of the ER-positive ratio between the WAs and CAs from 1990 to 2016. (D) Comparisons of the PR-positive ratio between the WAs and CAs from 1990 to 2016. (E) Comparisons of the insurance rate between the WAs and CAs from 2007 to 2016. (F) Comparisons of breast-conserving therapy ratio between the WAs and CAs from 1975 to 2016. (G) Comparisons of the ductal carcinoma in situ (DCIS) ratios between the WAs and CAs from 1975 to 2016. (H) Comparisons of 10-year overall survival (OS) between the WAs and CAs from 1975 to 2016.

Additionally, the tumor size (P < .001) was significantly variable for the WAs and CAs. But the ER and PR status did not significantly vary. And the percentage of the tumors below 4 cm of the WAs increased gradually from 2004 to 2016 (Fig. 2B), while that of the CAs fluctuated between 68% and 79%. The DCIS ratio of the CAs was much higher than that of the WAs (Table 1).

Besides that, the ER-positive rate of both the WAs and CAs started to increase in 2002, with a peak in 2014 (Fig. 2C). And the PR-positive rate presented similar patterns in Figure 2D. And the insurance ratio of the CAs was significantly higher (P < .001) than that of the WAs (Fig. 2E) with both groups above 96%.

In Figure 2F, from the 1970s to the mid-1990s, the WA breastconserving ratio increased steadily and reached 50% in 1994, while it remained around 60% in the next years. However, the breast-conserving rate of the CAs fluctuated due to the insufficient patients (<20 people) before the 1990s. But the overall trend of the CAs' breast-conserving rate was similar to that of the whites, and it was finally stable at around 60%.

3.2. Comparison of DCIS ratios between WAs and CAs

Further analysis showed that the differences of DCIS ratios between the WAs and CAs for each time interval achieved statistical significance (P < .001 for 1985–1994, 1995–2004, 2005–2016, and P < .05 for 1975–1984). As for the trend, a slight growth of DCIS ratios of both the WAs and CAs has been reflected from 1975 to 2000 (Fig. 2G) probably due to the mammographic screening program. Then, the DCIS ratios of both the WAs and CAs decreased from 2006 to 2016.

3.3. Comparison of the OS and prognosis between the WAs and CAs

Since the number of CA patients was limited before the 1990s, the statistics from 1989 (Fig. 2H) were analyzed. After the median follow-up of 129 months, 15,261 deaths were reported among patients in this study. The 10-year BCSS of the white and the CAs were 99.16% and 99.57% (Table 1, P = .038), with 308 and 371 months of the median overall survival, respectively. The prognosis of the CAs was significantly better than that of the White. Analysis of Kaplan–Meier survival curves with the logrank test revealed that both the OS and BCSS of CAs were superior to those of the whites (P < .001; P = .038) (Fig. 3).

Univariate and multivariate Cox proportional hazard regression models were used to identify the independent predictors in the DCIS patients. The results for BCSS and OS were present in Tables 2 and 3, respectively. Diagnosis of year 1995 to 2004 (HR, 0.607; 95% CI, 0.485, 0.760; P < .001) and 2005 to 2016 (HR, 0.552; 95% CI, 0.391, 0.778; P=.001), and BCT (HR, 0.864; 95% CI, 0.765, 0.976; P=.019) were independently associated with better BCSS in the analysis (Table 2). Findings were similar for OS except for the Chinese group and high family income (Table 3). Chinese group was independently associated with better OS (HR, 0.684; 95% CI, 0.593–0.789; P < .001) while the BCSS was not statistically distinct between the two groups (univariate P = .040, multivariate P = .113). Similarly, high family income (HR, 0.789; 95% CI, 0.740, 0.840; P < .001) was an independent positive factor for OS. These analyzes also showed that older age (HR, 1.800; 95% CI, 1.389, 2.334; P < .001) was an independent negative factor for BCSS, together with PRnegative subtype (HR, 1.512; 95% CI, 1.139, 2.006; P=.004)



Figure 3. Kaplan–Meier estimates of overall survival (OS, A) breast cancerspecific survival (BCSS, B) between Chinese Americans and White Americans.

and tumor ≥ 4 cm (HR, 1.627; 95% CI, 1.061, 2.494; P=.026). The result of OS was similar except the presence of Medicaid. Medicaid was an independent negative factor for OS (HR, 1.797; 95% CI, 1.504, 2.148; P<.001). Of note, there was no significant difference between the Cox result with the "Other" or "Unknown" groups preserved and the result without the "Other" or "Unknown" groups.

4. Discussion

Recently, the screening strategy has been recommended for women, resulting in a dramatically increased incidence of DCIS, especially in developed countries.^[1–5,12,21–25] US-residing Chinese women are the largest Asian American ethnic group and the fastest-growing immigrant group in the US. However, there have been no studies focused on the demographic, clinicopathologic, and survival factors of DCIS in Chinese Americans. In this study, the differences of DCIS characteristics between the WAs and CAs were analyzed and summarized to reveal the DCIS in CAs. Out data included DCIS cases of the period before the screening mammography and after it. Since the widespread adoption of screening mammography in the USA in the later 1980s,^[8] the DCIS ratio of CAs increased the same as that of whites.

DCIS has the potential to develop into invasive tumors, but the risk of dying from invasive breast cancer of DCIS patients is

Table 2

Univariate and multivariate Cox analyzes of breast cancer-specific survival.

	Univariate		Multivariate	
Variables	Hazard ratio	Р	Hazard ratio	Р
Year				
1975–1984	Reference		Reference	
1985–1994	0.732 (0.589,0.910)	.005	0.737 (0.591,0.919)	.007
1995–2004	0.580 (0.469,0.717)	<.001	0.607 (0.485,0.760)	<.001
2005–2016	0.398 (0.310,0.511)	<.001	0.552 (0.391,0.778)	.001
Age				
<40	Reference		Reference	
40–54	0.632 (0.490,0.816)	<.001	0.685 (0.530,0.884)	.004
55–69	0.889 (0.691,1.142)	.356	0.945 (0.735,1.215)	.659
>69	1.730 (1.336,2.241)	<.001	1.800 (1.389,2.334)	<.001
Race				
White	Reference		Reference	
Chinese	0.606 (0.375,0.978)	.040	0.697 (0.431,1.126)	.140
Tumor size				
<4 cm	Reference		Reference	
<u>≥</u> 4 cm	1.705 (1.116,2.605)	.014	1.627 (1.061,2.494)	.026
Other	1.634 (1.364,1.959)	<.001	1.246 (0.984,1.579)	.068
Estrogen receptor (1990+)				
Positive or borderline	Reference		Reference	
Negative	1.330 (1.046,1.690)	.020	0.896 (0.659,1.217)	.483
Unknown	1.272 (1.098,1.473)	<.001	0.793 (0.514,1.224)	.296
Progesterone receptor (1990+)				
Positive or borderline	Reference		Reference	
Negative	1.570 (1.258,1.959)	<.001	1.512 (1.139,2.006)	.004
Unknown	1.405 (1.194,1.653)	<.001	1.280 (0.823,1.993)	.274
Insurance				
Insured	Reference		Reference	
Medicaid	0.995 (0.437,2.268)	.991	1.013 (0.444,2.310)	.976
Not insured	2.212 (0.546,8.968)	.266	2.610 (0.643,10.590)	.180
Insurance status unknown	1.823 (1.467,2.265)	<.001	1.467 (1.096,1.962)	.010
Median Family Income (\$)				
<55,210	Reference		Reference	
55,211-64,460	1.083 (0.858,1.366)	.504	1.030 (0.815,1.302)	.804
64,461-78,500	0.916 (0.723,1.160)	.465	0.900 (0.710,1.142)	.387
>78,500	0.825 (0.657,1.036)	.098	0.816 (0.647,1.028)	.084
Surgery pattern				
Mastectomy without radiotherapy	Reference		Reference	
BCT	0.735 (0.656,0.825)	<.001	0.864 (0.765,0.976)	.019

Values in parentheses are 95% confidence intervals.

BCSS=breast cancer-specific survival, BCT=breast-conserving surgery with radiation therapy, ER=estrogen receptor, PR=progesterone receptor.

low.^[26] However, due to the fear of recurrence, there was an increase in mastectomy for early breast cancer in some countries, especially the USA.^[27] A similar trend was also present in China.^[28,29] Mastectomy remains the most popular surgical option for breast cancer, however, BCT showed superior breast cancer specific-survival than mastectomy in recent studies.^[30–35] Our analysis supported previous studies with a similar result. We discovered that DCIS patients of both WAs and CAs benefited from BCT in both univariate and multivariate analyzes. Besides the comparable effect with mastectomy, BCT has the psychological benefits over mastectomy.^[36,37] Considering the lower rate of BCT in CAs, BCT should be recommended for CA DCIS patients when both BCT and mastectomy are appropriate treatment alternatives.

Previous studies determined that there was no significant difference in breast cancer tumor biology between Chinese women in the US and Caucasian whereas the Chinese patients had a significantly better OS.^[38] However, in our analysis of

83,814 DCIS patients registered by the SEER program, we discovered that DCIS cases of CAs presented younger patients, smaller tumors, higher ER- and PR-positive rate with better OS compared with WAs. But the BCSS of Chinese groups was not statistically superior to that of the whites. Possible explanations for the differences between this study and prior study include:

- 1. this study was focused on the DCIS and the former study was focused on all breast cancer;
- 2. there is a high chance of survival for DCIS patients, tumor characteristics included in this study were unable to make a difference in the BCSS as ER-negative subtype was not independently associated with worse BCSS in this study;
- 3. the prior study excluded BC patients before 1990 and our study involved patients from 1975 to 2016.

Because the BCSS of CAs was not significantly superior to that of the whites in our study, the difference in OS was not due to breast cancer-related deaths. In this study, the ratio of younger DCIS

Table 3

Univariate and multivariate Cox analyzes of overall survival.

	Univariate		Multivariate	
Variables	Hazard ratio	Р	Hazard ratio	Р
Year				
1975–1984	Reference		Reference	
1985–1994	0.934 (0.876,0.995)	.034	0.874 (0.820,0.932)	<.001
1995–2004	0.829 (0.777,0.884)	<.001	0.817 (0.764,0.874)	<.001
2005–2016	0.687 (0.637,0.741)	<.001	0.800 (0.722,0.888)	<.001
Age				
<40	Reference		Reference	
40–54	1.606 (1.375,1.876)	<.001	1.666 (1.426,1.947)	<.001
55–69	5.943 (5.107,6.915)	<.001	6.116 (5.256,7.118)	<.001
>69	23.967 (20.588,27.900)	<.001	24.262 (20.840,28.245)	<.001
Race				
White	Reference		Reference	
Chinese	0.551 (0.478,0.635)	<.001	0.705 (0.611,0.813)	<.001
Tumor size				
<4 cm	Reference		Reference	
≥4 cm	1.141 (0.993,1.312)	.063	1.156 (1.005,1.331)	.042
Other	1.248 (1.186,1.314)	<.001	1.064 (0.993,1.139)	.077
Estrogen receptor (1990+)				
Positive or borderline	Reference		Reference	
Negative	1.199 (1.115,1.289)	<.001	1.049 (0.953,1.154)	.333
Unknown	1.223 (1.171,1.277)	<.001	1.229 (1.064,1.420)	.005
Progesterone receptor (1990+)				
Positive or borderline	Reference		Reference	
Negative	1.243 (1.163,1.329)	<.001	1.045 (0.957,1.141)	.327
Unknown	1.233 (1.177,1.292)	<.001	0.848 (0.733,0.981)	.026
Insurance				
Insured	Reference		Reference	
Medicaid	1.676 (1.403,2.001)	<.001	1.797 (1.504,2.148)	<.001
Not insured	0.916 (0.506,1.658)	.772	1.480 (0.818,2.680)	.195
Insurance status unknown	1.337 (1.257,1.422)	<.001	1.136 (1.044,1.237)	.003
Median family income (\$)				
<55,210	Reference		Reference	
55,211-64,460	0.899 (0.843,0.958)	.001	0.906 (0.850,0.967)	.003
64,461-78,500	0.769 (0.721,0.821)	<.001	0.843 (0.790,0.900)	<.001
>78,500	0.705 (0.662,0.750)	<.001	0.789 (0.740,0.840)	<.001
Surgery pattern				
Mastectomy without radiotherapy	Reference		Reference	
BCT	0.736 (0.712,0.760)	<.001	0.832 (0.803,0.861)	<.001

Values in parentheses are 95% confidence intervals.

BCT = breast-conserving surgery with radiation therapy, ER = estrogen receptor, OS = overall survival, PR = progesterone receptor.

patients of Chinese women was higher than that of WAs, which is consistent with the former study.^[39,40] It might be caused by a rapid increase in younger-aged individuals in the CAs in the latter half of the twentieth century.^[41] Thus, possibly Chinese patients might have few complications and better access to appropriate treatment due to their younger ages, higher income and favorable insurance status, resulting in superior OS than the whites. Another explanation was that the Chinese group might be influenced by the traditional Chinese lifestyle with reduced fat intake in some degree. Furthermore, there might be some confounding factors affecting breast cancer outcomes between these two groups. But due to the limited events of Chinese DCIS patients in the US, an over-fit bias might be present in the stratification analysis. Thus, we failed to perform a stratification analysis.

Recent two studies^[39,42] suggested that the DCIS characteristics of China women displayed several distinct patterns from US patients. The tumor characteristics of DCIS in US-residing Chinese might be similar to the women living in China. However,

in our study, Chinese Americans also appeared to be of higher social-economic status than that of the whites. And the insurance rate of the CA group was distinctly higher than the whites, suggesting that they had access to appropriate medical insurance. According to the influence of the SES and environmental factors on the BC survival,^[43] we suggest that the survival outcome of DCIS of women living in China may be improved with nationwide screening programs and advanced treatment. Additionally, despite the DCIS ratio in Chinese women in the US showed a general increase in our study, most DCIS ratio reported in China remained very low, with the median ratio of 6.8%, even in the developed areas.^[15,44–48] Since 2009, cervical and breast cancer screening service has been launched in China. However, a recent study reported that the BC screening program in China only covered 22.5% of the targeted women and the coverage among women residing in rural and central or western China was lower than those in urban or eastern China.^[49] Thus, it is urgent to strengthen BC screening programs in China.

This study had the advantage of including a sizable number of DCIS patients reported to cancer registries with near completeness in registration and follow-up of cancer patients.^[50] Besides, our study was the first to compare the DCIS features between Chinese women in the US and white women and we focused on an understudied population: Chinese American DCIS patients. Furthermore, we tried to provide some clues for the future status of DCIS in mainland China.

However, our study also had some traditional shortages. Considering this was a retrospective study of which the allocation of patients to receive BCT or mastectomy is not random, bias was inevitable. The different sample size between the Chinese group and the white group was also one of the limitations of this study. The statistical validity might be limited by the number of CAs. And the SEER histology code was based on the pathology report rather than diagnostic results before surgery. We cannot determine the effect of the diagnostic accuracy on patients' treatment preferences. Another limitation was the possible disparities between Chinese immigrants and US-born Chinese. Considering that both immigrants and US-born Chinese were assigned to the CA group, we cannot analyze and rule out the influence caused by their differences. Additionally, we failed to reveal the local recurrence rate due to the lack of information in the SEER program.

In summary, our study demonstrated that CA patients had improved breast cancer-specific survival compared with their white counterparts for DCIS and BCT provided benefits for both groups. These findings deserve to be validated by further preclinical and clinical studies and the underlying mechanisms need to be explored.

Acknowledgments

We appreciated it that the Website Support Team from SEER at the National Cancer Institute kindly provided us with free access to the data.

Author contributions

Conceptualization: Xin-Wen Kuang, Chuang Chen.

Data curation: Xin-Wen Kuang, Zhi-Hong Sun.

Formal analysis: Zhi-Hong Sun.

Investigation: Jun-Long Song, Zhanyong Zhu.

Methodology: Jun-Long Song.

Supervision: Zhanyong Zhu, Chuang Chen.

Writing - original draft: Xin-Wen Kuang, Zhi-Hong Sun.

Writing – review & editing: Xin-Wen Kuang, Zhi-Hong Sun, Jun-Long Song, Zhanyong Zhu, Chuang Chen.

References

- Virnig BA, Tuttle TM, Shamliyan T, et al. Ductal carcinoma in situ of the breast: a systematic review of incidence, treatment, and outcomes. J Natl Cancer Inst 2010;102:170–8.
- [2] Partridge AH, Elmore JG, Saslow D, et al. Challenges in ductal carcinoma in situ risk communication and decision-making: report from an American Cancer Society and National Cancer Institute workshop. CA Cancer J Clin 2012;62:203–10.
- [3] Bremer T, Whitworth PW, Patel R, et al. A Biological signature for breast ductal carcinoma in situ to predict radiotherapy benefit and assess recurrence risk. Clin Cancer Res 2018;24:5895–901.
- [4] Benson JR, Wishart GC. Predictors of recurrence for ductal carcinoma in situ after breast-conserving surgery. Lancet Oncol 2013;14:e348–57.

- [5] DeSantis CE, Ma J, Goding Sauer A, et al. Breast cancer statistics, 2017, racial disparity in mortality by state. CA Cancer J Clin 2017;67:439–48.
- [6] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin 2018;68:7–30.
- [7] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin 2019;69:7–34.
- [8] DeSantis CE, Ma J, Gaudet MM, et al. Breast cancer statistics, 2019. CA Cancer J Clin 2019;69:438–51.
- [9] Hofvind S, Vacek PM, Skelly J, et al. Comparing screening mammography for early breast cancer detection in Vermont and Norway. J Natl Cancer Inst 2008;100:1082–91.
- [10] Lynge E, Ponti A, James T, et al. Variation in detection of ductal carcinoma in situ during screening mammography: a survey within the International Cancer Screening Network. Eur J Cancer 2014;50:185–92.
- [11] Ward EM, DeSantis CE, Lin CC, et al. Cancer statistics: breast cancer in situ. CA Cancer J Clin 2015;65:481–95.
- [12] Jacklyn G, Morrell S, McGeechan K, et al. Carcinoma in situ of the breast in New South Wales, Australia: current status and trends over the last 40 year. Breast 2018;37:170–8.
- [13] van Maaren MC, Lagendijk M, Tilanus-Linthorst M, et al. Breast cancerrelated deaths according to grade in ductal carcinoma in situ: a Dutch population-based study on patients diagnosed between 1999 and 2012. Eur J Cancer 2018;101:134–42.
- [14] Onega T, Weaver DL, Frederick PD, et al. The diagnostic challenge of low-grade ductal carcinoma in situ. Eur J Cancer 2017;80:39–47.
- [15] Wang L, Zhang W, Lyu S, et al. Clinicopathologic characteristics and molecular subtypes of microinvasive carcinoma of the breast. Tumour Biol 2015;36:2241–8.
- [16] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–32.
- [17] Li Y, Zhang S, Wei X, et al. The clinical features and management of women with ductal carcinoma in situ with microinvasion: a retrospective Cohort study. Int J Surg 2015;19:91–4.
- [18] Jobsen JJ, Scheijmans L, Smit W, et al. Breast-conserving therapy for primary Ductal Carcinoma in situ in the Netherlands: a multi-center study and population-based analysis. Breast 2018;42:3–9.
- [19] Zhu SJ, Chen XS, Wu JY, et al. Surgical treatment and prognosis of ductal carcinoma in situ: 526 cases analysis. Chin J Surg 2017;55:114–9.
- [20] Elizabeth M. Hoeffel SR, Myoung Ouk Kim HS. The Asian Population: 2010: U.S. Census Bureau; 2012.
- [21] Hofvind S, Sørum R, Haldorsen T, et al. Incidence of breast cancer before and after implementation of mammography screening. Tidsskr Nor Laegeforen 2006;126:2935–8.
- [22] Feig SA. Ductal carcinoma in situ. Implications for screening mammography. Radiol Clin North Am 2000;38:653–68. vii.
- [23] Demers AA, Turner D, Mo D, et al. Breast cancer trends in Manitoba: 40 years of follow-up. Chronic Dis Can 2005;26:13–9.
- [24] Johnson A, Shekhdar J. Breast cancer incidence: what do the figures mean. J Eval Clin Pract 2005;11:27–31.
- [25] Jonsson H, Johansson R, Lenner P. Increased incidence of invasive breast cancer after the introduction of service screening with mammography in Sweden. Int J Cancer 2005;117:842–7.
- [26] Narod SA, Iqbal J, Giannakeas V, et al. Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol 2015;1:888–96.
- [27] Kummerow KL, Du L, Penson DF, et al. Nationwide trends in mastectomy for early-stage breast cancer. JAMA Surg 2015;150:9–16.
- [28] Yau TK, Soong IS, Sze H, et al. Trends and patterns of breast conservation treatment in Hong Kong: 1994-2007. Int J Radiat Oncol Biol Phys 2009;74:98–103.
- [29] Huang NS, Liu MY, Chen JJ, et al. Surgical management of breast cancer in China: A 15-year single-center retrospective study of 18,502 patients. Medicine (Baltimore) 2016;95:e4201.
- [30] Baxter NN, Virnig BA, Durham SB, et al. Trends in the treatment of ductal carcinoma in situ of the breast. J Natl Cancer Inst 2004;96:443–8.
- [31] de Boniface J, Frisell J, Bergkvist L, et al. Breast-conserving surgery followed by whole-breast irradiation offers survival benefits over mastectomy without irradiation. Br J Surg 2018;105:1607–14.
- [32] Worni M, Akushevich I, Greenup R, et al. Trends in treatment patterns and outcomes for ductal carcinoma in situ. J Natl Cancer Inst 2015;107: djv263.
- [33] Mazor AM, Mateo AM, Demora L, et al. Breast conservation versus mastectomy in patients with T3 breast cancers (>5 cm): an analysis of 37,268 patients from the National Cancer Database. Breast Cancer Res Treat 2019;173:301–11.

- [34] Fisher S, Gao H, Yasui Y, et al. Survival in stage I-III breast cancer patients by surgical treatment in a publicly funded health care system. Ann Oncol 2015;26:1161–9.
- [35] Agarwal S, Pappas L, Neumayer L, et al. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. JAMA Surg 2014;149:267–74.
- [36] Anderson C, Islam JY, Elizabeth Hodgson M, et al. Long-term satisfaction and body image after contralateral prophylactic mastectomy. Ann Surg Oncol 2017;24:1499–506.
- [37] Ng ET, Ang RZ, Tran BX, et al. Comparing quality of life in breast cancer patients who underwent mastectomy versus breast-conserving surgery: a meta-analysis. Int J Environ Res Public Health 2019;16:4970.
- [38] Chen DN, Song CG, Ouyang QW, et al. Differences in breast cancer characteristics and outcomes between Caucasian and Chinese women in the US. Oncotarget 2015;6:12774–82.
- [39] Iqbal J, Ginsburg O, Rochon PA, et al. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States. JAMA 2015;313:165–73.
- [40] Li J, Zhang BN, Fan JH, et al. A nation-wide multicenter 10-year (1999-2008) retrospective clinical epidemiological study of female breast cancer in China. BMC Cancer 2011;11:364.
- [41] Gathani T, Ali R, Balkwill A, et al. Ethnic differences in breast cancer incidence in England are due to differences in known risk factors for the disease: prospective study. Br J Cancer 2014;110:224–9.
- [42] Sun X, Wang YS, Chen P, et al. Sentinel lymph node biopsy for patients with breast ductal carcinoma in situ. Chin J Clin Oncol 2012;39:1652–5.

- [43] Quaglia A, Lillini R, Casella C, et al. The combined effect of age and socio-economic status on breast cancer survival. Crit Rev Oncol Hematol 2011;77:210–20.
- [44] Kong Y, Yang L, Tang H, et al. A nation-wide multicenter retrospective study of the epidemiological, pathological and clinical characteristics of breast cancer in situ in Chinese women in 1999-2008. PLoS One 2013;8: e81055.
- [45] Zhang W, Gao EL, Zhou YL, et al. Different distribution of breast ductal carcinoma in situ, ductal carcinoma in situ with microinvasion, and invasion breast cancer. World J Surg Oncol 2012;10:262.
- [46] Yuan XM, Wang N, Ouyang T, et al. Current status of diagnosis and treatment of primary breast cancer in Beijing, 2008. Chin J Cancer Res 2011;23:38–42.
- [47] Ming XU, Hui YE, Manna YE, et al. [Analysis of Pathological and Immunohistochemical Features of Breast Ductal Carcinoma in Situ with Microinvasion]. Chin J Clin Med 2015;2:224–7.
- [48] Yao JJ, Zhan WW, Chen M, et al. Sonographic features of ductal carcinoma in situ of the breast with microinvasion: correlation with clinicopathologic findings and biomarkers. J Ultrasound Med 2015;34:1761–8.
- [49] Bao HL, Wang LH, Wang LM, et al. Study on the coverage of cervical and breast cancer screening among women aged 35-69 years and related impact of socioeconomic factors in China, 2013. Chin J Epidemiol 2018;39:208–12.
- [50] Chow WH, Shuch B, Linehan WM, et al. Racial disparity in renal cell carcinoma patient survival according to demographic and clinical characteristics. Cancer 2013;119:388–94.