

A multi-center investigation of breast-conserving surgery based on data from the Chinese Society of Breast Surgery (CSBrS-005)

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Abstract

Background: Although breast-conserving surgery is one of the standard treatments for breast cancer, few studies have assessed its recent implementation in China. We aimed to clarify the current real-world status of breast-conserving surgery in China.

Methods: This cross-sectional survey relied on data collected by the Chinese Society of Breast Surgery (CSBrS) to examine patients who underwent this surgery between January 2018 and December 2018. The survey was conducted using a uniform electronic questionnaire to collect information, including clinical and pathological data on these patients.

Results: Overall, 4459 breast-conserving surgeries were performed in 34 member units of CSBrS, accounting for 14.6% of all breast cancer surgeries performed in these units during the study period. In patients who underwent breast-conserving surgery with information on tumor size available, more than half (61.2%) of the tumors were smaller than 2 cm in diameter, and only 87 (3.2%) tumors were larger than 4 cm in diameter. Among patients who underwent breast-conserving surgeries, 457 (10.2%) patients received neoadjuvant therapy before the surgery. Among patients with a reported margin width, 34 (2.0%) patients had a margin of ≤ 2 mm, and 1530 (88.2%) of them had a margin of > 5 mm.

Conclusions: This study demonstrated the rates of breast-conserving surgery in member units of the CSBrS, and introduced the characteristics and surgical margins of patients who underwent this surgery. This information helps describe the real-world status of breast-conserving surgery in China.

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Keywords: Breast cancer; Breast-conserving surgery; Multi-center research; Real-world study

Introduction

After several clinical studies confirmed the efficacy of breast-conserving surgery,^[1,2] the National Institutes of Health recommended it as an appropriate treatment method for early-stage breast cancer in 1991.^[3] Early randomized clinical trials using large sample sizes found that breast-conserving surgery yielded comparable survival rates and better cosmetic outcomes compared to radical surgery.^[1,4] A recent study showed that early-stage breast cancer patients who underwent breast-conserving surgery plus radiotherapy had a better 10-year overall and relative survival than those who underwent a mastectomy.^[5] Due to its excellent clinical and cosmetic outcomes, breast-conserving surgery has been accepted as one of the standard treatments for early-stage breast cancer over the past 30 years.

Currently, several academic organizations in China actively promote breast-conserving surgery and have successively established relevant guidelines.^[6,7] Some hospitals in South China, such as the Sun Yat-sen Memorial Hospital, had a breast-conserving surgery rate of more than 50%, which was close to the rate observed in developed countries.^[8] However, the overall rate of breast-conserving surgery in China was still low.^[9,10] Treatment-related decisions can be influenced by multiple factors, including clinician preferences, concerns about recurrence, and additional treatment requirements. The “no ink on tumor” or negative margin guideline may also affect the implementation of breast-conserving surgery.^[11] However, in recent years, few studies have examined the characteristics of patients who underwent breast-conserving surgeries in China. The Chinese Society of Breast Surgery (CSBrS) conducted a multi-center cross-sectional survey of breast-conserving surgeries based

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Table 1: Rates of breast-conserving surgery by geographic regions.

Region	Breast-conserving surgery, <i>n</i>	Surgeries of breast cancer, <i>n</i>	Breast-conserving rate (%)
Northeast China	540	6052	8.9
North China	872	3743	23.3
East China	1122	8019	14.0
South China	631	1341	47.1
Central China	592	4145	14.3
Northwest China	241	2213	10.9
Southwest China	461	4981	9.3
Total	4459	30,494	14.6

on the member units. Using data from this survey, we aimed to clarify the current real-world status of breast-conserving surgery in a Chinese population and to provide a reference for the formulation of relevant strategies.

Methods

Ethical approval

The study was performed in accordance with the *Declaration of Helsinki* and was approved by the Ethics Committee of the Second Hospital of Shandong University (No. KYLL-2019 (KJ) P-0082). As this was a retrospective study and all data analyses were performed anonymously, the need for informed consent from patients was waived.

Study population

This study relied on data collected by CSBrS to investigate patients who underwent breast-conserving surgeries from January 2018 to December 2018. All patients included in the study were (a) women, (b) breast cancer patients from member hospitals of CSBrS, and (c) diagnosed with breast cancer pathologically and had undergone breast-conserving surgery. The exclusion criteria were: (a) occurrence of distant metastases before surgery, (b) inflammatory breast cancer, and (c) male breast cancer. The survey was conducted using a uniform, electronic questionnaire, which included questions regarding the general conditions and clinical-pathological data of the patients. The clinical-pathological data included information on the tumor location (side and quadrant), tumor size, neoadjuvant therapy, mode of lymph node surgery, pathological type, molecular subtype, and margin width. Data were obtained through the electronic medical record system of each hospital. The molecular subtypes including luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)+, and triple-negative breast cancer were based on the expression of the estrogen receptor, progesterone receptor, HER2, and Ki-67 according to the European Society for Medical Oncology 2015 Primary Breast Cancer Clinical Practice Guidelines.^[12] All investigators received uniform training from the CSBrS. Data collection was completed by June 31, 2019.

Statistical analysis

After the collection of data, the logic was checked, and outliers were removed. The general information on

the clinical and pathological data from patients undergoing breast-conserving surgeries was evaluated. The areas of hospitals covered in this study were divided into seven regions: Northeast China, North China, East China, South China, Central China, Northwest China, and Southwest China according to the registering regions of the National Central Cancer Registry of China.^[13] Data were presented as numbers and percentages. SPSS version 20.0 software (IBM, Armonk, NY, USA) was used for statistical analyses.

Results

Rates of breast-conserving surgery

Questionnaires were sent to 40 member units of the CSBrS, and 34 of them responded by providing the required data. According to the responses, a total of 30,494 breast cancer patients underwent surgery from January 2018 to December 2018, and 4459 (14.6%) of those had breast-conserving surgeries. Hospitals in South China reported the highest rate of breast-conserving surgery (47.1%), while those in Northeast China reported a rate of only 8.9% [Table 1].

Characteristics of patients

The mean age of patients who underwent breast-conserving surgery was 48.7 ± 11.2 years. While 855 (19.8%) patients were <40 years of age, only 100 (2.3%) of them were over 75 years of age. The proportion of premenopausal and postmenopausal patients was 58.2% and 41.8%, respectively. The tumor was located on the left side in 1863 (51.5%) patients, and in the lateral upper quadrant in 1387 (49.4%) patients. Among the patients, 139 (5.3%) reported a family history of breast cancer, and 197 (7.9%) had a family history of malignant tumors [Table 2].

In patients who reported information regarding tumor size ($n = 2754$), 1684 (61.2%) of the tumors were smaller than 2 cm in diameter, and only 87 (3.2%) patients had tumors larger than 4 cm in diameter. Among these patients, 457 (10.2%) patients received neoadjuvant therapy before surgery, 2932 (80.7%) patients underwent sentinel lymph node biopsy, and 2284 (76.9%) patients had negative axillary lymph nodes. In terms of pathological type, invasive ductal carcinomas (IDCs) accounted for 63.8% of

Table 2: Characteristics of patients who underwent breast-conserving surgery.

Characteristics	Breast-conserving surgery, n (%)
Age (years)	4319
<40	855 (19.8)
40–49	1662 (38.5)
50–65	1481 (34.4)
66–75	221 (5.1)
>75	100 (2.3)
Menstrual status	3535
Premenopausal	2056 (58.2)
Postmenopausal	1479 (41.8)
Number of births	3049
0	173 (5.7)
1–2	2684 (88.0)
≥3	192 (6.3)
Family history of breast cancer	2641
No	2502 (94.7)
Yes	139 (5.3)
Family history of malignant tumors	2481
No	2284 (92.1)
Yes	197 (7.9)
Tumor side	3616
Left	1863 (51.5)
Right	1733 (47.9)
Bilateral	20 (0.6)
Tumor quadrant	2806
Lateral upper quadrant	1387 (49.4)
Lateral lower quadrant	603 (21.5)
Interior upper quadrant	503 (17.9)
Interior lower quadrant	264 (9.4)
Areola area	49 (1.7)
Tumor size	2754
≤1 cm	349 (12.7)
1 cm < size ≤ 2 cm	1335 (48.5)
2 cm < size ≤ 3 cm	806 (29.3)
3 cm < size ≤ 4 cm	177 (6.4)
>4 cm	87 (3.2)
Neoadjuvant therapy	4459
No	4002 (89.8)
Yes	457 (10.2)
Axillary surgery	3632
SLNB	2932 (80.7)
ALND	700 (19.3)
Number of metastatic nodes	2969
0	2284 (76.9)
1–3	526 (17.7)
4–9	116 (3.9)
≥10	43 (1.4)
Pathological type	3957
IDC	2523 (63.8)
ILC	100 (2.5)
DCIS	436 (11.0)
LCIS	32 (0.8)
Other subtypes	866 (21.9)
Molecular subtype	3768
Luminal A	875 (23.2)
Luminal B	2186 (58.0)
HER2+	229 (6.1)
TNBC	478 (12.7)

SLNB: Sentinel lymph node biopsy; ALND: Axillary lymph node dissection; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; DCIS: Ductal carcinoma *in situ*; LCIS: Lobular carcinoma *in situ*; HER2: Human epidermal growth factor receptor 2; TNBC: Triple-negative breast cancer.

the tumors, while ductal carcinomas *in situ* (DCIS) accounted for 11.0% of the tumors [Table 2].

Surgical margins of patients

Among patients who reported information regarding surgical margins ($n=3119$), 227 (7.3%) of them had positive margins at the first time and underwent extended excision until the margins were negative. Among patients who reported the margin width ($n=1734$), 34 (2.0%) of them had a margin ≤ 2 mm, and 1530 (88.2%) had a margin of >5 mm. Among patients with a margin of ≤ 2 mm, 21 (1.9%) had IDCs, and 1 (0.7%) had DCIS [Table 3].

Discussion

Breast-conserving surgery has been accepted as a standard treatment for early-stage breast cancer.^[14] It is used to treat more than 50% of patients with early breast cancer in western countries.^[15,16] The present study found that the rate of breast-conserving surgeries in member units of the CSBrS was 14.6%. Although the rate had increased since 2008 (11.88%) based on a multi-center study in China,^[9] our findings suggest that this rate should continue to increase further. This surgery was reported at a rate of 8.9% in Northeast China and 47.1% in South China, illustrating regional differences in the acceptance of breast-conserving surgery by doctors and patients.

The rate of breast-conserving surgeries is reported to be low in some low- and middle-income countries due to the advanced stage at diagnosis.^[17,18] In recent years, with advances in screening technology and health awareness, the detection of early breast cancer in China has increased.^[19] However, the rate of detection is still low compared to that in developed countries,^[20,21] which was an important factor limiting the implementation of breast-conserving surgery in China. Neoadjuvant therapy is an important strategy to improve the rate of breast-conserving surgery, and its safety was confirmed in the TBCRC017 study.^[22] The NSABP B18 study demonstrated comparable long-term survival rates in patients who underwent neoadjuvant chemotherapy followed by breast-conserving surgery when compared to those who underwent early breast-conserving surgery.^[23] This study also showed that only 10.2% of Chinese patients underwent breast-conserving surgery after neoadjuvant therapy, which was lower than the proportion reported in developed countries.^[23,24] Patients play a vital role in the choice of surgery for breast cancer, and nearly 80% of them were directly or indirectly involved in choosing the surgical approach.^[25] Concerns regarding the risk of recurrence and the effects of post-operative radiation therapy made patients more likely to choose mastectomy over breast-conserving surgery.^[25] A questionnaire survey investigated 1264 patients with early-stage breast cancer in China and found that only 7.3% of them anticipated undergoing breast-conserving surgery.^[26] This was primarily due to an insufficient understanding of the safety of breast-conserving surgery, and concerns about local recurrence after the surgery. In such cases, recommendations from doctors were particularly important.

Table 3: Information on surgical margins in patients who underwent breast-conserving surgery.

Characteristics	Breast-conserving surgery, n (%)	IDC, n (%)	DCIS, n (%)
Positive residual tumor margin for the first time, n = 3119			
No	2892 (92.7)	1436 (92.3)	305 (90.8)
Yes	227 (7.3)	120 (7.7)	31 (9.2)
Margin width, n = 1734			
≤1 mm	7 (0.4)	2 (0.2)	1 (0.7)
1 mm < width ≤ 2 mm	27 (1.6)	19 (1.7)	0 (0)
2 mm < width ≤ 5 mm	170 (9.8)	77 (6.8)	14 (10.3)
>5 mm	1530 (88.2)	1027 (91.3)	121 (89.0)

IDC: Invasive ductal carcinoma; DCIS: Ductal carcinoma *in situ*.

A negative surgical margin is an indicator of successful breast-conserving surgery. Studies have confirmed that positive margins following breast-conserving surgery increase the risk of local recurrence requiring re-operation.^[27] This, in turn, may result in poor cosmetic appearance and increased complications and financial burden.^[27] However, among patients with negative margins, a wider margin did not reduce the local recurrence rate.^[28] In 2014, the Society of Surgical Oncology and American Society for Radiation Oncology recommended the “no ink on tumor” guideline to be the standard for negative margins in breast-conserving surgery.^[29] The overall re-excision rates declined significantly after the adoption of this guideline.^[30] In the present study, the incidence of a close margin (≤1 mm) was 0.4%, which was lower than that reported by the Memorial Sloan Kettering Cancer Center.^[30] The incidence of cases with margins >5 mm was 88.2%, which was comparable to that reported in a study from Denmark (93%).^[28] These findings indicate that the majority of Chinese patients who underwent breast-conserving surgery had a margin of >5 mm. The rate of initial positive margins was 7.3% in this study, which was lower than that observed in developed countries.^[29] This indicates that Chinese doctors were relatively conservative with margins during breast-conserving surgeries and that a wide range of glands was removed. Currently, in China, the margins for breast-conserving surgeries are determined based on the intraoperative frozen pathology. Moreover, these surgeries require longer intraoperative waiting periods and; therefore, add to the workload of breast surgeons and pathologists. At the same time, the overall follow-up rate for breast cancer in China is low. Therefore, without timely regular re-examinations, relapse after a breast-conserving surgery might not be detected until the terminal stage. These factors limit the extensive use of breast-conserving surgery in the absence of sufficient human resources and advanced medical technology.

The present study has some limitations that require consideration. First, the hospitals enrolled in this study were all members of the CSBrS. All of them were third-grade hospitals, providing relatively high-quality health care services. The overall rate of breast-conserving surgeries performed in the included hospitals was 14.6%, which may be possibly higher than the nationwide rate. Second, this study only collected the general, clinical, and pathological data from patients who underwent breast-conserving surgery. We could not analyze differences in the rates of

breast-conserving surgeries in different patients. Finally, considerable data were missing for some variables. Tumor size and margin width were reported for only 2754 (61.8%) and 1734 (38.9%) cases, respectively, which might affect the results of this study.

In conclusion, this study demonstrated the rates of breast-conserving surgery in member units of the CSBrS and introduced the characteristics and surgical margins of patients who underwent this surgery. It was helpful to understand the real-world status of breast-conserving surgery in China. The attitude of doctors and patients towards breast-conserving surgery was conservative in some hospitals. Efforts to improve the expertise of breast surgeons are required to standardize the breast-conserving surgery procedure and increase its implementation in China.

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Conflicts of interest

None.

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