

Clinical practice guideline for breast-conserving surgery in patients with early-stage breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021.

Title: Clinical practice guideline for breast-conserving surgery in patients with early-stage breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021.

Publication year: 2021

Journal: Chinese medical journal

Authors: Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, Guangdong 510120, China.

Society: European Respiratory Society

Origin country: International (Europe)

Target countries: Europe

DOI: 10.1097/CM9.0000000000001518

PMID: 34133359

Source: <https://pubmed.ncbi.nlm.nih.gov/34133359/>

pmc Chin Med J (Engl) Chin Med J (Engl) 2337 chinesemj 7513795 CM9 Chinese Medical Journal 0366-6999 2542-5641 Wolters Kluwer Health PMC8478397 PMC8478397.1 8478397 8478397 34133359 10.1097/CM9.0000000000001518 CMJ-2021-128 1 Clinical Guideline Clinical practice guideline for breast-conserving surgery in patients with early-stage breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021 Chen Kai 1 2 Liu Jie-Qiong 1 2 Wu Wei 1 2 Su Feng-Xi 1 2 Zou Qiang 3 Song Er-Wei 1 2 Chinese Society of Breast Surgery Yin Yan-Jie Hao Xiu-Yuan 1 Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, Guangdong 510120, China 2 Department of Breast Surgery, Yat-sen Breast Tumor Hospital, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, China 3 Department of Surgery, Huashan Hospital, Fudan University, Shanghai 200040, China. Correspondence to: Dr. Er-Wei Song, Department of Breast Surgery, Yat-sen Breast Tumor Hospital, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong 510120, China E-Mail: songew@mail.sysu.edu.cn Dr. Qiang Zou, Department of Surgery, Huashan Hospital, Fudan University, Shanghai 200040, China E-Mail: zouqiang003@aliyun.com 20 9 2021 16 6 2021 134 18 390910 2143 2146 14 1 2021 20 09 2021 30 09 2021 06 05 2024 Copyright © 2021 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. 2021 <https://creativecommons.org/licenses/by-nc-nd/4.0/> This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. <http://creativecommons.org/licenses/by-nc-nd/4.0> pmc-status-qastatus 0 pmc-status-live yes pmc-status-embargo no pmc-status-released yes pmc-prop-open-access yes pmc-prop-olp no pmc-prop-manuscript no pmc-prop-legally-suppressed no pmc-prop-has-pdf yes pmc-prop-has-supplement no pmc-prop-pdf-only no pmc-prop-suppress-copyright no pmc-prop-is-real-version no pmc-prop-is-scanned-article no pmc-prop-preprint no pmc-prop-in-epmc yes pmc-license-ref CC BY-NC-ND OPEN-ACCESS TRUE Breast-conserving surgery (BCS) with radiotherapy is the primarily agreed surgical choice for eligible patients with an early diagnosis of breast cancer. In 2019, the panel of Chinese experts assembled by the Chinese Society for Breast Surgery (CSBrS) developed a Chinese experts' consensus on BCS for early-stage breast cancer (Version 2019) with the aim of standardizing BCS in China. Subsequently, the CSBrS conducted a review of published reports and discussions between experts to determine the key clinical questions for the Clinical Practice Guideline for BCS in

Patients with Early-Stage Breast Cancer. The group evaluated the relevant evidence using the grading of recommendations assessment, development, and evaluation system, and developed a Clinical Practice Guideline for BCS in Patients with Early-Stage Breast Cancer (Version 2021), with the aim of providing guidance on clinical practice to breast surgeons in China.

The panel for this guideline is comprised of 85 experts, including 70 (82.3%) breast surgeons, four (4.7%) medical oncologists, four (4.7%) diagnostic radiologists, two (2.4%) pathologists, one (1.2%) obstetrician, two (2.4%) radiation oncologists, and two (2.4%) epidemiologists.

Clinicians specializing in breast diseases in China.

Recommendation 1: Indications (all of the indications should be met).

Recommendation 2: Contraindications (any one of the indications is sufficient).

Whole-breast irradiation can be waived in patients aged >65 years with Stage I breast cancer, hormone receptor-positive tumors, and negative surgical margins (CALGB9343 trial).

A considerable amount of evidence from the scientific literature supports the safety and efficacy of combining BCS with radiotherapy in the early stages of breast cancer. In the National Surgical Adjuvant Breast and Bowel Project B-06 trial, a total of 1851 patients diagnosed with Stage I or II breast cancer were randomly allocated to three study arms, namely total mastectomy, BCS, and BCS with radiotherapy. According to results of the long-term follow-up that lasted 20 years, it was found that disease-free survival, metastasis-free survival, and overall survival did not differ significantly between the three arms. [4] During the same period, in the Milan I trial, seven hundred and one patients with <T2 breast cancers (tumor size measuring <2 cm) were randomized to two arms: radical mastectomy and BCS with radiotherapy. The 20-year follow-up results indicated that there was no significant difference between the overall survival of the two arms. However, the cumulative recurrence rate was higher in the BCS + radiation arm (8.8%) when compared with the mastectomy arm (2.3%). [5] A short-term follow-up study of 95 Chinese patients by Li et al [22] revealed that, after an average follow-up of 17 months, the 2-year local recurrence rate of Stage I or II breast cancer after BCS was only 1.4%, with no metastases or deaths. Chen et al [16] used propensity-score matching to compare the clinical outcomes after a median follow-up of 67 months of 2866 patients with early-stage breast cancer who had undergone BCS or mastectomy in China; they confirmed the safety and efficacy of BCS. Recently, BCS has been recommended internationally as the standard surgical treatment for eligible breast cancer patients in the early stages. [2 , 3 , 8] The panel members agreed that, provided acceptable cosmetic outcomes could be expected, BCS is suitable for patients with clinical Stage I or II disease or ≤T2 tumors who wish to preserve their breasts.

The result of Early Breast Cancer Trialists' Collaborative Group meta-analysis revealed that neoadjuvant chemotherapy can significantly increase the BCS rate. The 10-year cumulative local recurrence rate was slightly, but not significantly, higher in the neoadjuvant chemotherapy than in the untreated group (15.1% vs . 11.9%, $P = 0.10$). No significant differences were observed in the 10-year cumulative rates of breast cancer-related deaths between patients who did and did not receive neoadjuvant chemotherapy (27.5% vs . 24.8%, $P = 0.15$). [23] Therefore, for patients who were clinically diagnosed with Stage III breast cancer or >T2 tumors, it is possible to administer neoadjuvant chemotherapy to downstage the tumor, and thus increase the chances of being eligible for BCS. The panel members considered that, in clinical practice, it is not always easy to accurately measure the degree of shrinkage of a tumor after neoadjuvant chemotherapy. Thus, there was a lack of consensus in the panel regarding the optimal extent of surgery in patients with breast cancer who have received neoadjuvant chemotherapy. However, there was agreement that achieving negative surgical margins is mandatory in this situation.

The panel considered that the following factors are potential risk factors for local recurrence after BCS: breast cancer located in the central portion; bloody discharge from the nipple; large tumor (eg, >T2); multifocal breast cancer; multicentric breast cancer; young age (<35 years); and radiotherapy contraindicated (eg, active connective tissue disease). However, there is no high level evidence that the abovementioned factors are contraindications to BCS.

Achieving negative surgical margins is mandatory for successful BCS. There is evidence that positive surgical margins are closely associated with local recurrence. [2 , 8 , 9 , 24] Intra-operative gross inspection, [25] imprint cytology, [26] intra-operative specimen imaging, [27] and novel devices [28 , 29] can also reportedly reduce the rates of positive margins. However, the panel does not recommend these approaches because of the lack of high-level evidence. Intra-operative frozen section analysis (FSA) is reportedly capable of reducing the rates of margin positivity and second surgeries. [30] The panel considers that FSA is widely used in clinical practice in China and supports its use for intra-operative margin assessment. The panel take a cautious attitude toward performing margin assessment only by post-operative formalin-fixed, paraffin-embedded examination.

Both lumpectomy margins and cavity margins are suitable for the margin assessment of BCS. Lumpectomy margins are assessed on the surface of the tumor-containing specimen. There are two techniques that can be used for margin assessment: the perpendicular inked and tangential shaved techniques. [2 , 14] Cavity margins are assessed by performing a biopsy (tissue sampling) of the residual cavity (or the wall of the tumor bed) after tumor removal. Well-designed studies suggesting that cavity margin assessment alone is capable of achieving excellent local control have been published. [15 , 19]

A meta-analysis has demonstrated that the “no-ink on tumor” is significantly associated with a reduced local recurrence rate and that wider surgical margins do not further improve the local control rate. [31] Furthermore, the increased risk of local recurrence associated with positive surgical margins is not nullified by post-operative radiotherapy. There is no evidence that different margin widths should be considered for patients of different ages or with different molecular subtypes. A real-world study (CSBrS-005) conducted by the CSBrS in 2019 revealed that 88.2% (1530/1734) of patients who had undergone BCS had margin widths >5 mm. [32] Others have reached consensus on diagnosing negative surgical margins for infiltrating ductal carcinoma and ductal carcinoma in situ by “no-ink on tumor” and “≥2 mm,” respectively. [2 , 3 , 7] The panel considered these standards inappropriate for China and has not recommended them for routine use.

The panel agreed that whole-breast irradiation (RT) is necessary after BCS. However, the CALGB9493 trial showed a small improvement of locoregional recurrence rate in BCS patients who received RT (RT: 2% (95% confidence interval [CI]: 1% to 4%) vs. no-RT: 10% (95% CI: 7% to 15%)), but no statistically significant differences in 10-year distant metastasis and overall survival between patients with low-risk BCS who did and did not undergo RT. [33] In contrast, the PRIME II trial showed that, in patients aged ≥65 years with early-stage and hormone receptor-positive disease who underwent BCS, the 5-year ipsilateral recurrence rates were 4.1% and 1.3% (P = 0.0002) in the no-RT and RT groups, respectively. [34] Although this difference is statistically significant, the benefit is not clinically important. The panel suggested that RT might be forgone after BCS in certain situations related to the patients' preferences and comorbidities.

The International Breast Cancer Study Group VI-VII trial [35] aimed to analyze how the timing of RT affects the local failure rate and disease-free survival (DFS) in breast cancer patients. Among pre/perimenopausal patients, the 15-year DFSs were 48.2% vs . 44.9% (hazard ratio [HR] = 1.12, 95% CI: 0.87–1.45) in patients allocated 3 and 6 months of initial chemotherapy (CT). Among post-menopausal patients, the 15-year DFS was 46.1% and 43.3% in the group that did not receive CT initially and the group allocated 3 months of CT, respectively (HR 1.11, 95% CI: 0.82–1.51). The results of this clinical trial suggest that delaying RT until after completion of CT is safe and reasonable. The panel recommended that whole-breast RT is indicated for eligible breast cancer

patients after BCS and CT.

The CO-HO-RT trial [36] revealed that the risk of developing grade ≥ 2 radiation-induced subcutaneous fibrosis is similar in patients who receive concurrent vs . sequential RT and endocrine therapy, suggesting that concurrent use of these treatment modalities is safe. According to the 3.7-year follow-up data of the N9831 trial, [37] concurrent use of RT and trastuzumab did not significantly increase cardiotoxicity, supporting the feasibility of the concurrent use of RT and anti-human epidermal growth factor receptor 2 (HER2) treatments. The panel recommended the concurrent use of RT and endocrine therapy, as well as anti-HER2 therapy if indicated.

The authors thank Dr. Trish Reynolds, MBBS, FRACP, from Liwen Bianji, Edanz Group China (www.liwenbianji.cn/ac), for editing the English draft of this manuscript. The authors thank Jia-Fan Ma for revision of this manuscript.

List of compiling committee members (In alphabetical order by surname): Zhong-Wei Cao, De-Dian Chen, Kai Chen, Yuan-Jia Cheng, Xue-Ning Duan, Zhi-Min Fan, Pei-Fen Fu, Jian Huang, Jun Jiang, Hong-Chuan Jiang, Feng Jin, Hua Kang, Rui Ling, Jin-Ping Liu, Jie-Qiong Liu, Ke Liu, Qian Liu, Yin-Hua Liu, Yun-Jiang Liu, Zhen-Zhen Liu, Yong-Hui Luo, Rong Ma, Da-Hua Mao, Jiang-Hua Ou, Xiang Qu, Guo-Sheng Ren, Ai-Lin Song, Er-Wei Song, Feng-Xi Su, Li-Li Tang, Xing-Song Tian, Chuan Wang, Fei Wang, Jian-Dong Wang, Shu Wang, Shui Wang, Xiang Wang, Jiong Wu, Ke-Jin Wu, Wei Wu, Fei Xie, Ling Xin, Zhi-Gang Yu, Jian-Guo Zhang, Jin Zhang, Jing-Hua Zhang, Yi Zhao, Zuo-Wei Zhao, Ang Zheng, Wei Zhu, Qiang Zou

The expert committee for these guidelines declares no conflict of interest.

These guidelines are a reference for breast disease specialists in clinical practice. However, the guidelines are not to be used as the basis for medical evaluation, and do not play an arbitrating role in the handling of any medical disputes. The guidelines are not a reference for patients or non-breast specialists. The Chinese Society of Breast Surgery assumes no responsibility for results involving the inappropriate application of these guidelines, and reserves the right to interpret and revise the guidelines.

How to cite this article: Chen K, Liu JQ, Wu W, Su FX, Zou Q, Song EW, Chinese Society of Breast Surgery. Clinical practice guideline for breast-conserving surgery in patients with early-stage breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021. Chin Med J 2021;134:2143–2146. doi: 10.1097/CM9.0000000000001518