

Clinical practice guidelines for pregnancy-associated breast cancer: Chinese society of breast surgery (CSBrS) practice guidelines 2021.

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pmc Chin Med J (Engl) Chin Med J (Engl) 2337 chinesemj 7513795 CM9 Chinese Medical Journal 0366-6999 2542-5641 Wolters Kluwer Health PMC8654448 PMC8654448.1 8654448 8654448 34456258 10.1097/CM9.0000000000001686 CMJ-2021-889 1 Consensus Statement Clinical practice guidelines for pregnancy-associated breast cancer: Chinese society of breast surgery (CSBrS) practice guidelines 2021 Chen Qing 1 Qiu Yi-Ran 2 Zhang Ming-Di 1 Zhu Wei 3 Gu Wei-Rong 4 Wu Ke-Jin 1 Yin Yan-Jie Hao Xiu-Yuan 1 Department of Breast Surgery, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China 2 Shanghai Medical College, Fudan University, Shanghai 200032, China 3 Department of General Surgery, Zhongshan Hospital of Fudan University, Shanghai 200032, China 4 Department of Obstetrics, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, China. Correspondence to: Dr. Ke-Jin Wu, Department of Breast Surgery, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200011, ChinaE-Mail: kejinwu@163.com Dr. Wei Zhu, Department of General Surgery, Zhongshan Hospital of Fudan University, Shanghai 200032, ChinaE-Mail: drzhu@163.com 20 10 2021 27 8 2021 134 20 395297 2395 2397 29 3 2021 20 10 2021 10 12 2021 11 12 2021 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-olf 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 Pregnancy-associated breast cancer (PABC), including breast cancer during pregnancy (BCP) and postpartum breast cancer (PBC), has become a critical issue for clinicians in consideration of both maternal and offspring safety during diagnosis and treatment. The recommendations in this guideline are mainly based on currently available high-quality prospective studies, retrospective cohort studies, meta-analyses, and guidelines and consensus documents published by internationally recognized or national societies or associations. Clinicians should carefully analyze the potential benefits and risks of each treatment before recommending whether to terminate the pregnancy or lactation, balance the advantages and disadvantages of the treatments, and respect the wishes of patients.

There were 77 members in the Voting Committee of this guideline, including 63 (81.8%) in breast surgery, one (1.3%) in obstetrics, three (3.9%) in oncology, four (5.2%) in medical imaging, two (2.6%) in pathology, two (2.6%) in radiotherapy, and two (2.6%) in epidemiology.

Clinicians specializing in breast diseases in China.

The diagnostic method of PBC is same as that of non-pregnancy-associated breast cancer (non-PABC).

The treatment principle of PBC is the same as that of non-PABC.

* Timing of radiotherapy should be fully considered.

Currently, most publications suggest that PABC refers to breast cancer diagnosed during pregnancy, that is, BCP, and breast cancer diagnosed within 1 year after delivery, that is, PBC. [3] In addition to breastfeeding, the diagnosis and treatment principles of PBC can refer to those of non-PABC. This guidance involves more principles of BCP.

Most Chinese women have dense mammary glands, and tissue congestion and swelling of the gland during pregnancy leads to further increases of gland density. Therefore, the expert group recommends breast ultrasound to assess the breasts and axillary lymph nodes of pregnant women. [2] Because high-level evidence supporting the clinical value of breast X-ray during pregnancy is lacking, the expert group has not made specific recommendations. Gadolinium-based contrast agents for breast-enhanced magnetic resonance imaging (MRI) can penetrate the blood-placenta barrier and potentially cause teratogenicity, [7] and thus, breast-enhanced MRI is forbidden during pregnancy. NCCN Clinical Practice Guidelines in Oncology (2020) clearly indicated that computed tomography and radionuclide scanning are forbidden during pregnancy. [4] Based on the literature evidence, the expert group has proposed that patients with BCP can choose abdominal ultrasound and chest X-ray examination under abdominal shielding as screening modalities for distant metastasis. [2 , 4 , 5] However, clinicians must pay attention to the possibility of insufficient assessment of distant metastatic lesions because of the limited options for imaging examinations for pregnant women. Experts from the American College of Radiology believe that breast ultrasound is the first option for breast examination in lactating women, and breast X-ray or MRI can be used as a supplement. [8]

For patients with breast imaging-reporting and data system (BI-RADS) 4 or 5 in breast imaging or those with BI-RADS 3 and risk factors, core needle biopsy (CNB) for histopathological assessment has been widely accepted. [3] The expert group recommends that pregnant or lactating women without contraindications should undergo CNB to obtain histopathological diagnosis.

It must be emphasized that surgical stress response and anticancer drugs may affect the developing fetus. Studies demonstrated that in early pregnancy (gestational week $\leq 13 + 6$) breast cancer surgery increases the risk of abortion, and chemotherapy leads to a fetal malformation rate of 20%. [5] The expert group believes that the treatment plan for patients in early pregnancy requires special caution. Treatment plans should be devised in consideration of the clinical stage, biological characteristics of the tumor, and gestational period of the patients. Individualized management of patients via multidisciplinary treatment should be emphasized, and their wishes should be fully respected. It has been reported that the termination of pregnancy cannot improve the prognosis of BCP in the second and third trimesters, and breast cancer can be treated according to the condition. [3 – 5]

Modified radical mastectomy for breast cancer is a standard surgical procedure for patients with BCP. [4 – 6] The survival rates of patients with stage I or II BCP after breast-conserving surgery and mastectomy are similar. [6] Owing to the clear risk of teratogenesis to the fetus induced by radiotherapy, [5] the expert group suggests that the timing of post-operative radiotherapy should

be fully considered before breast-conserving surgery. Sulfur colloid labeled with the sentinel lymph node biopsy tracer ^{99m}Tc is relatively safe for the developing fetus, [9] but the level of evidence is not high. [10] Blue dye tracers may cause maternal allergic reactions and their safety in pregnant women is unclear. [4 – 5] Because of the change of the shape of the breast during pregnancy and increase of the duration of anesthesia, the expert group does not recommend primary breast reconstruction for patients with BCP. The principle of PBC surgery can refer to that of non-PABC, but clinicians should pay attention to the possibility of morphological changes in the breast during lactation and carefully choose breast-conserving surgery and primary reconstruction surgery.

The expert group cited a lack of long-term follow-up data for patients receiving chemotherapy during pregnancy and neonatal outcomes, and the use of chemotherapy during pregnancy should be carefully considered. Studies illustrated that chemotherapy may lead to gestational hypertension, fetal intrauterine growth restriction, neonatal weight loss, and premature delivery. [6] Chemotherapy in early pregnancy can lead to premature delivery and malformation. [5] For patients with BCP who must receive chemotherapy, it is suggested to discuss their data with obstetricians, improve the screening of fetal malformations, and devise the chemotherapy plan after joint assessment. In principle, chemotherapy is recommended in the second and third trimesters of pregnancy. [4 – 6] After 35 weeks of gestation or within 3 weeks before planned delivery, chemotherapy should not be performed to avoid hematological complications during delivery. [3 – 5]

Anthracycline-based chemotherapy can be carefully considered for patients with BCP. [5 – 6] Taxanes have been recognized by the European Society for Medical Oncology, [5] but the NCCN Clinical Practice Guidelines in Oncology (2020) indicated that there are insufficient safety data to support the recommendation of routine use of paclitaxel during pregnancy. [4] Tamoxifen endocrine therapy, anti-Her-2 targeted therapy and radiotherapy are not recommended in patients with BCP or in those with PBC during breastfeeding and breastfeeding is also not preferred during chemotherapy. [3 – 5]

Patients with PABC are usually younger, and thus, the possibility of hereditary breast cancer should be considered to guide fertility and risk management related to hereditary breast cancer in the next generation. In addition to regular follow-up in the breast department, it is suggested to include follow-up in children's health care and other specialties and generate long-term follow-up data on the health status of infants receiving prenatal treatment to accumulate follow-up data for two generations.

Zhong-Wei Cao, De-Dian Chen, Qing Chen, Yuan-Jia Cheng, Xuan-Ning Duan, Zhi-Min Fan, Pei-Fen Fu, Wei-Rong Gu, Jian Huang, Jun Jiang, Hong-Chuan Jiang, Feng Jin, Hua Kang, Rui Ling, Jin-Ping 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, Yi-Ran Qiu, Xiang Qu, Guo-Sheng Ren, Ai-Lin Song, Er-Wei Song, Li-Li Tang, Xing-Song Tian, Chuan Wang, Fei Wang, Jian-Dong Wang, Shu Wang, Shui Wang, Xiang Wang, Jiong Wu, Ke-Jin Wu, Fei Xie, Ling Xin, Zhi-Gang Yu, Jian-Guo Zhang, Jin Zhang, Jing-Hua Zhang, Ming-Di Zhang, Yi Zhao, Zuo-Wei Zhao, Wei Zhu, Ang Zheng, and 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.

We state that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

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