

Clinical practice guidelines for the diagnosis and treatment of inflammatory breast cancer: Chinese Society of Breast Surgery (CSBrS) Practice Guidelines 2022

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To improve the diagnosis and treatment of inflammatory breast cancer (IBC), the Chinese Society of Breast Surgery (CSBrS) of the Chinese Medical Association identified the key clinical issues for clinical practice guidelines through literature research and evaluated the relevant evidence with reference to the Grading of Recommendations Assessment, Development and Evaluation (GRADE).^[1]

Level of evidence standard and recommendation strength criteria are shown in previous publication.^[2] Recommendation strength review committee was comprised of 31 members and all the members are breast surgeons. The target audience are Chinese breast disease specialists. The recommendation is shown in Table 1.

The American Joint Committee of Cancer (AJCC) 8th edition of breast cancer staging criteria clearly states that the diagnosis of IBC is mainly based on clinical manifestations, and it emphasizes the basic features of “diffuse erythema and edema changes” and “involving at least 1/3 of the skin of the breast.” With or without a potentially palpable mass, the history did not last more than 6 months.^[3] It is recommended that patients who meet the diagnostic criteria for IBC undergo at least two skin punch biopsies, especially in the absence of metastatic lesions in breast parenchyma or regional lymph nodes.^[4]

The expert panel emphasized the importance of physical examination and topical medical photographs in assessing IBC efficacy to help determine the extent of skin involvement for surgical excision and for subsequent radiotherapy.^[5] The 2018 International Consensus on the Clinical Management of Inflammatory Breast Cancer recommends that all patients with suspected IBC undergo mammography, B-ultrasound of the breast and regional lymph nodes, and magnetic resonance imaging (MRI).

The 2021 National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines recommend plain computed tomography (CT) imaging of the chest and pelvis and enhanced CT imaging of the abdomen for patients with clinically/pathologically diagnosed IBC (Category 2B evidence), plain CT imaging of the chest when pulmonary symptoms are present (Class 2A evidence), and bone scan or fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT (Class 2B evidence) to determine the presence of distant metastases.^[6]

The 2018 International Consensus and the US NCCN guidelines recommended neoadjuvant chemotherapy, modified radical mastectomy, and adjuvant radiotherapy as the main treatments for non-metastatic IBC.^[5,6]

Trastuzumab + pertuzumab combined with chemotherapy is the standard neoadjuvant therapy for patients with *HER2*-positive IBC. Evidence supporting this regimen was mainly derived from the NOAH^[7] and KRISTINE studies.^[8] For patients with *HER2*-negative IBC, most consensus recommend initial treatment with anthracene- and taxane-based chemotherapy.^[3,5,6]

The surgical indications for IBC recommended by MD Anderson Cancer Center include stage III IBC if significant clinical efficacy is observed after neoadjuvant therapy. If the clinical efficacy of neoadjuvant therapy is poor, then systematic treatment regimens and preoperative radiotherapy may be considered.^[9] The value of surgery in patients newly diagnosed with stage IV IBC is controversial, and the evidence of an OS benefit is particularly lacking. The main purpose of surgical treatment for patients with newly diagnosed stage IV IBC is to improve the local control rate and reduce the tumor load.^[10] The incision design should refer to the scope of the

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Table 1: Recommendation for the diagnosis, auxiliary examination, and treatment of inflammatory breast cancer.

Recommendation items	Level of evidence	Recommendation strength
Recommendation 1: Diagnostic criteria		
Typical clinical manifestations: rapid breast erythema, edema and/or orange skin change, and/or skin temperature rise; the lesion area comprises more than one-third of the breast; with or without a potentially palpable internal breast mass; the history did not last more than 6 months. ^[3,4]	I	Class A
Breast cancer was pathologically confirmed by skin biopsy or hollow needle biopsy. ^[3,4]	I	Class A
Recommendation 2: Auxiliary examination		
Local examination		
Physical examination	I	Class A
Mammography ^[5,6]	I	Class A
Ultrasonography of the breast and regional lymph nodes ^[5,6]	I	Class A
Breast MRI ^[5]	I	Class A
General examination		
Nuclide scanning or FDG-PET/CT ^[6]	II	Class A
Cranial/chest/abdominal/pelvic enhanced CT/MRI ^[6]	I	Class A
Recommendation 3: Treatment		
Basic principle	I	Class A
Multidisciplinary collaboration, systemic therapy is preferred ^[5,6]		
Systemic therapy	I	Class A
Treatment is selected according to AJCC (8th edition) clinical TNM stage and molecular typing for breast cancer ^[5]		
HER2+: Chemotherapy regimen based on trastuzumab combined with pertuzumab and other anti-HER2 drugs ^[6-8]	II	Class A
HER2-: Chemotherapy regimen based on anthracene and taxanes ^[3,5,6]	II	Class A
Surgery		
Indications	I	Class A
Preoperative treatment regimen ≥ 4 cycles, the efficacy evaluation is a clinical partial response or clinical complete response according to the RECIST (1.1) standard, clinical prediction of non-initial stage IV IBC with R0 excision of breast lesions, ^[6,9] with stable disease control, surgery can significantly improve the quality of life of stage IV IBC ^[10]		
Surgical procedure		
Modified radical mastectomy ^[5,6]	I	Class A
Evaluation of skin margin in frozen pathological sections ^[11]	II	Class A
Contraindications of breast-conserving surgery ^[5,6]	I	Class A
Contraindications of sentinel lymph node biopsy ^[5,6]	I	Class A
Radiation therapy		
Indications		
IBC after R0 resection ^[5,6]	I	Class A
Sites		
No significant response to neoadjuvant therapy without surgery ^[12]	II	Class A
After R0 resection: chest wall, ipsilateral clavicle, and inner mammary area ^[5,6]	I	Class A
No surgery: whole breast + lymphatic drainage area ^[12]	II	Class A
Dose		
Conventional dose: pCR: 50 Gy; non-pCR: 51 Gy. Additional dose: 15 Gy or 16 Gy ^[5]	II	Class A
Preoperative radiotherapy: 45–50 Gy, palliative radiotherapy: residual lesion addition: 10–25 Gy ^[12]	II	Class A
Adjuvant endocrine therapy		
Premenopause: LHRHa + AI ^[13]	I	Class A
Postmenopause: AI ^[13]	I	Class A

Evidence level I: Based on high-level prospective randomized controlled clinical trials, observational studies or meta-analyses with large sample sizes; Evidence level II: Based on low-level randomized clinical trials, well-designed non-controlled trials or cohort studies. Recommendation Class A: Average total score for the four influencing factors (level of evidence, health economics, product equivalence, and accessibility): >80, B: 60–80, C: <60. AI: Aromatase inhibitor; AJCC: American Joint Committee on Cancer; FDG-PET/CT: Fluorodeoxyglucose positron emission tomography/computed tomography; HER2+: Human-epidermal growth factor receptor 2 positive; HER2-: Epidermal growth factor receptor 2 negative; IBC: Inflammatory breast cancer; LHRHa: Luteinizing hormone releasing hormone analogue; MRI: Magnetic resonance imaging; pCR: Pathologic complete response; RECIST: Response evaluation criteria in solid tumours; TNM: Tumor node metastasis.

initially diagnosed lesion, and the incision margin should be evaluated by the frozen pathological section.^[11]

Major international guidelines agree that IBC should be treated with radiotherapy after R0 resection.^[5,6] For patients with poor systemic treatment efficacy who cannot undergo surgical resection after the efficacy evaluation, preoperative radiotherapy can be considered after consultation with radiologists. If the efficacy of radio-

therapy remains poor, palliative radiotherapy can be considered to increase local control as much as possible.^[12]

MD Anderson and the Dana-Farber Institute for Cancer Research recommended radiotherapy targeting sites including the chest wall and supraclavicular, subclavian, and internal mammary lymph node regions in patients with IBC.^[5] Patients with internal mammary lymph node involvement should be given internal mammary

lymph node radiotherapy, even if there is no evidence of clinical involvement, and internal mammary lymph node radiotherapy can also be considered (level 3 evidence).^[6]

The MD Anderson Cancer Center recommended the following radiotherapy doses for IBC: 50 Gy for patients with pathologic complete response (pCR) following neoadjuvant chemotherapy who are younger than 45 years old and who have lesions close to the incision edge, and 51 Gy for patients with non-pCR who are receiving radiotherapy. The dosage at chest wall and draining lymph node area was recommended as 15–16 Gy.^[5] The guidelines for radiotherapy for breast cancer issued by the Chinese Medical Doctor Association suggest that the radiotherapy dose for unresectable IBC should be 45–50 Gy with conventional segmentation, and local surgical resection can be performed 4–6 weeks after radiotherapy. If local resection is still not feasible because of poor efficacy, simple palliative radiotherapy can be considered with an additional dose of 10–25 Gy for residual lesions.^[12]

Patients with hormone receptor-positive IBC should receive endocrine therapy, which can be implemented by referring to the plan for patients with non-IBC breast cancer with specific reference to CSCO Guidelines for Breast Cancer Diagnosis and Treatment 2021 issued by The Chinese Society of Clinical Oncology.^[13]

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Conflicts of interest

The Expert Committee for this guideline declares no conflict of interest. This guideline is intended to serve as a reference for the clinical work of physicians specializing in breast disease. It does not serve as a basis for medical evaluation, nor does it arbitrate on any medical disputes or controversies or serve as a reference for patients or non-breast specialists. The Chinese Society of Breast Surgery of the Chinese Medical Association does not assume any responsibility for any results involving the inappropriate application of this guideline, and it reserves the right to interpret and revise this guideline.

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