Chinese Expert Consensus on the Treatment of Breast Cancer in the Elderly (2018) Postprint

Authors: Chinese Expert Panel on Elderly Breast Cancer Treatment Consensus

Date: 2018-06-14T00:00:00+00:00

Abstract

Elderly breast cancer is seldom addressed in clinical research, and elderly patients frequently present with complex comorbidities, leading to considerable controversies and uncertainties in its clinical management. The Treatment Consensus Expert Group of the Breast Cancer Subcommittee of the Chinese Society of Geriatric Oncology, after comprehensive deliberation on the treatment of elderly breast cancer and adhering to the principle of "reaching consensus on critical issues while seeking common ground and reserving differences on contentious matters,"has developed this expert consensus on local therapy, adjuvant systemic therapy, salvage therapy, and neoadjuvant therapy for elderly breast cancer to serve as a reference for clinicians.

Full Text

Preamble

Medical Journal of Peking Union Medical College Hospital, ChinaXiv Cooperative Journal

Chinese Expert Consensus on the Treatment of Breast Cancer in Elderly Patients (2018)

Chinese Elderly Breast Cancer Treatment Consensus Expert Group

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Abstract: Elderly patients (aged 70 years) with breast cancer are seldom included in clinical trials. On the other hand, elderly patients often present with

complicated comorbidities. This has given rise to great controversies over the management of elderly breast cancer cases. Specialists from the Breast Cancer Committee of the Chinese Geriatric Oncology Society (CGOS) established principles of reaching consensus on key issues while reserving differences on controversial matters, in order to provide evidence-based recommendations for the treatment of breast cancer in elderly individuals. The recommendations include local and adjuvant systemic treatments for primary breast carcinoma in elderly patients, neoadjuvant therapy, and treatment approaches for recurrent elderly patients.

Keywords: elderly; breast carcinoma; treatment

1. Local Treatment of Elderly Breast Cancer

1.1 Breast-Conserving Surgery

Standard breast-conserving radical surgery should be performed after patients are fully informed about surgical risks and recurrence rates. Specific indications and contraindications such as lesion size, distance from the nipple, connective tissue disease, or cardiopulmonary conditions must be thoroughly considered preoperatively and discussed with patients.

For clinically axillary lymph node-negative elderly patients, the necessity of sentinel lymph node biopsy or axillary dissection has long been controversial. Several clinical studies have compared these approaches. Martelli et al. published 5-year follow-up results showing no statistically significant difference in prognosis between dissection and non-dissection groups (local recurrence rates 9.0% vs. 1.8%, $p>0.05$; distant metastasis rates 14.0% vs. 11.6%, $p>0.05$). The IBCSG 10-93 study with 15-year follow-up also demonstrated no significant differences in distant metastasis or breast cancer-related mortality between groups. However, quality of life was significantly improved in the non-dissection group. Current evidence suggests that for elderly breast cancer patients with clinically negative axillary nodes, particularly those with tumors <2 cm, axillary lymph node dissection may be omitted as these patients derive minimal survival benefit from axillary staging. The International Society of Geriatric Oncology and European Society of Breast Cancer Specialists have proposed similar recommendations in their guidelines, as subsequent treatment typically involves endocrine therapy alone, making axillary staging unnecessary for guiding adjuvant therapy strategies. Nevertheless, this conclusion requires further validation through prospective clinical trials.

Margin assessment, whether using perpendicular radial sectioning or shave techniques, must ensure tumor-free margins. For lesions identified as ductal carcinoma in situ (DCIS) on intraoperative frozen section or preoperative biopsy, margins should be expanded according to the 2016 American Society of Clinical Oncology guidelines to achieve a pathological margin distance 2 mm from the

tumor edge.

The necessity of postoperative radiotherapy after breast-conserving surgery in elderly patients remains controversial, though most experts lean toward omitting whole-breast radiation in selected cases. The CALGB 9343 study of hormone receptor-positive elderly patients who underwent breast-conserving surgery showed 10-year local recurrence rates of 2% with radiation versus 9% without (p=0.0002), though no significant differences were observed in regional metastasis, distant metastasis, or overall survival (93.9% in both groups). The PRIME II study included a slightly higher-risk population and demonstrated 5-year ipsilateral breast recurrence rates of 1.3% with radiation versus 4.1% without (p=0.0002). Given that the vast majority of elderly breast cancers are hormone receptor-positive, we recommend that for Chinese elderly patients with clinically negative axillary nodes, negative imaging studies, low-grade tumors <3 cm without lymphovascular invasion, endocrine therapy alone after breast-conserving surgery may be considered, omitting both axillary staging and postoperative radiation. However, for physically fit patients with longer life expectancy, the benefits of radiation in controlling local recurrence must be weighed against its side effects through individualized decision-making after thorough patient communication.

1.2 Modified Radical Surgery

For elderly patients in good physical condition with suspicious axillary lymph nodes, modified radical surgery may be selected after pathological confirmation (via core needle or open biopsy). Preoperative consultation with anesthesia and critical care departments is mandatory to assess tolerance to general anesthesia and manage comorbidities, with full communication of surgical benefits and risks to patients and families.

1.3 Alternative Approaches

In addition to surgical options, endocrine therapy alone represents a viable alternative for selected elderly patients. A 2007 systematic review examining hormone receptor-positive elderly breast cancer found no significant difference in overall survival between surgery plus tamoxifen versus tamoxifen alone, though disease-free survival favored the combined approach. For elderly patients with limited life expectancy or those unable/unwilling to undergo surgery due to anesthesia intolerance, primary endocrine therapy is a reasonable option.

2. Adjuvant Systemic Therapy

2.1 Endocrine Therapy

Multiple clinical studies have confirmed that aromatase inhibitors (AIs), whether used as initial therapy or sequentially after tamoxifen, provide superior risk reduction compared to tamoxifen alone in postmenopausal women. While

no randomized trials specifically targeting elderly female breast cancer patients have compared these strategies, data from large randomized controlled trials including elderly subgroups support extrapolating these findings to older populations. However, chronological and biological age often differ in elderly patients, requiring comprehensive assessment of performance status and life expectancy to guide treatment decisions.

Extended endocrine therapy beyond 5 years yields survival benefits primarily in patients under 70 years, suggesting limited value for routine extension in elderly patients. However, for fit elderly patients with advanced pathological stage and predicted endocrine sensitivity, individualized extended therapy may be considered. Compared to tamoxifen, AIs are associated with greater bone loss but lower risks of thrombotic events and endometrial cancer, with no significant difference in quality of life impact. The 2017 European Society for Medical Oncology guidelines recommend the Comprehensive Geriatric Assessment (CGA) system, though its 45-minute completion time and requirement for geriatric specialists limit clinical applicability. We recommend AIs as preferred agents, with tamoxifen reserved for patients with osteoporosis or cardiovascular risk factors.

2.2 Targeted Therapy

For HER2-positive elderly breast cancer, trastuzumab-based adjuvant therapy significantly reduces recurrence risk. Treatment duration is 1 year (8 mg/kg loading dose, then 6 mg/kg every 3 weeks; or 4 mg/kg loading dose, then 2 mg/kg weekly). Prerequisites include LVEF 50% and no history of structural heart disease. Cardiac function must be monitored every 3 months via echocardiography or MUGA scan. Although trastuzumab has demonstrated favorable safety over nearly two decades, with reversible cardiotoxicity unlike anthracyclines, elderly patients have diminished cardiac reserve. Treatment must be paused if LVEF drops below 50% or symptomatic heart failure develops, with dose adjustments based on weight and vigilant monitoring.

2.3 Chemotherapy

Chemotherapy in elderly patients requires careful risk-benefit assessment due to increased toxicity and organ dysfunction. Baseline evaluation should include complete blood counts and liver, kidney, and cardiac function tests, with informed consent after thorough communication. For fit elderly patients without comorbidities, standard regimens may be administered following general guidelines, including anthracycline-based (CAF, AC, CE120F, FE100C), taxane-based, or anthracycline-taxane sequential protocols. However, for patients with comorbidities or poor performance status, dose reductions or alternative regimens are warranted.

Single-agent capecitabine, while not standard adjuvant therapy, represents a valuable option for elderly patients unable to tolerate standard chemotherapy. The CALGB 49907 study demonstrated significantly better quality of life

with capecitabine compared to standard chemotherapy, albeit with inferior disease-free and overall survival. The FinXX and CREATE-X studies support capecitabine' s efficacy in adjuvant settings. Given its favorable toxicity profile and oral administration, capecitabine is recommended for elderly patients requiring chemotherapy but unable to tolerate standard regimens, with doses adjusted based on tolerance but not below recommended minimums.

3. Salvage Therapy and Neoadjuvant Therapy

3.1 Salvage Therapy

Management of metastatic breast cancer in elderly women generally follows standard population guidelines. For hormone receptor-positive disease, endocrine therapy is preferred first-line. The FALCON study showed fulvestrant 500 mg prolonged median PFS compared to anastrozole (16.6 vs. 13.8 months, HR=0.79, p=0.0486) in endocrine-naive patients. For AI-resistant disease, options include fulvestrant, tamoxifen, or exemestane plus everolimus. Progression after three sequential endocrine regimens suggests resistance, warranting cytotoxic therapy.

For elderly metastatic patients requiring chemotherapy, capecitabine is recommended as first-line therapy based on the OMEGA study, which showed comparable efficacy but superior tolerability and quality of life compared to liposomal doxorubicin. Single-agent chemotherapy is preferred over combination regimens due to better tolerability, with options including taxanes, vinorelbine, gemcitabine, or oral capecitabine. The balance between survival benefit, quality of life, and tolerability is paramount in this population.

3.2 Neoadjuvant Therapy

3.2.1 Indications and Objectives Indications for neoadjuvant therapy in elderly patients mirror those for the general population, primarily to render inoperable tumors resectable. Unlike younger patients where breast conservation is a key goal, elderly patients typically undergo neoadjuvant therapy to reduce tumor burden when lesions involve skin, chest wall, or fixed axillary nodes. Treatment should be promptly discontinued and surgery performed once operability is achieved to avoid resistance development.

3.2.2 Treatment Selection For elderly patients in good condition, standard chemotherapy regimens may be used. However, for those with poor performance status or comorbidities, single-agent oral chemotherapy is preferable. Hormone receptor-positive patients should receive primary endocrine therapy, while hormone receptor-negative disease requires cytotoxic agents. HER2-positive patients may receive trastuzumab concurrently with chemotherapy.

3.2.3 Monitoring and Assessment Baseline imaging evaluation should precisely measure primary tumor and axillary lymph node dimensions (sum of

longest diameters for multiple lesions). Core needle biopsy of the primary lesion is required for histological and immunohistochemical diagnosis, with cytology for suspicious nodes. Response assessment combining physical examination and imaging should occur after each treatment cycle (every 1-2 weeks for chemotherapy, monthly for endocrine therapy). Patients achieving operable status should proceed to surgery, while those with progression after two cycles require treatment modification. Postoperative adjuvant therapy should follow standard guidelines.

4. Screening Recommendations

The American Cancer Society' s classic guidelines recommended annual mammography and clinical breast examination for women aged 40+, which were revised in 2015 to annual screening for average-risk women starting at age 45, with biennial screening acceptable for those 55+. While China lacks universal screening coverage, we recommend annual breast evaluation for elderly women, combining ultrasound and mammography with self-examination and clinical palpation, to enhance early detection awareness and improve outcomes.

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Note: Figure translations are in progress. See original paper for figures.