Research In Cancer and Tumor 2026, 13(2): 19-22
DOI: 10.5923/j.rct.20261302.01

Personalized Approach to Chemotherapy for Breast Cancer in Elderly Women Based on Biological Subtypes (Literature Review)

L. T. Alimkhodjaeva, O. M. Akhmadjanova, S. S. Ziyavidenova

Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology, Tashkent, Uzbekistan

Abstract **The aim** of the study was to conduct a systematic analysis of literature data on the efficiency of chemotherapy for breast cancer in elderly women based on biological subtypes. The most common malignant tumor is breast cancer, which ranks first among all malignant tumors in women. Although the extent of the malignant process is the most important criterion for prognosis and the selection of a treatment strategy, its correlation with treatment efficiency and disease outcome is not always detected. Patients with hormone-sensitive and HER2-amplified tumor subtypes have a better short-term prognosis than those with hormone-negative and Erb-B2-overexpressing ones. The only systemic therapy that is beneficial for triple-negative breast cancer is chemotherapy, and it should be used in patients who are in good physical condition.

Keywords Breast cancer, Targeted and systemic chemotherapy, Luminal A subtype, Luminal B subtype, HER2 protein

1. Introduction

The most common malignant tumor is breast cancer (BC), which ranks first among all malignant tumors in women. Although the extent of the malignant process is the most important criterion for prognosis and the selection of a treatment strategy, its correlation with treatment efficiency and disease outcome is not always detected. Recently, a number of molecular markers of tumor cells have been included in the list of prognostic criteria [1-3]. Among patients aged 65 and older, most tumors are characterized by positive steroid hormone receptor expression (ER+) and HER2-negative (HER2-) status: these are luminal A-subtype tumors, which are characterized by a favorable clinical course and outcome, a later age at onset, a high degree of differentiation, a low Ki67 proliferation index, and a relatively favorable prognosis compared to hormone-receptor-negative tumors. This type is also characterized by a low recurrence rate and a long life duration [4-5]. It responds well to hormone therapy in both neoadjuvant and adjuvant regimens and, as a rule, to neoadjuvant chemotherapy. As we know, the luminal A subtype is characterized by low proliferative activity and, as a result, low sensitivity to adjuvant chemotherapy; therefore, the main treatment options are surgery and hormone therapy, with or without radiation therapy.

Received: Aug. 28; Accepted: Sep. 22, 2026; Published: Oct. 28, 2026
Published online at http://journal.sapub.org/rct

The aim of the study was to conduct a systematic analysis of literature data on the efficiency of chemotherapy for breast cancer in elderly women based on biological subtypes.

2. Materials and Methods

This study was conducted as a systematic literature review. A search for publications was conducted in PubMed/ MEDLINE, Scopus, Web of Science, Google Scholar, and eLibrary for the period 2010–2015, including select earlier studies that retained methodological and clinical relevance. The search strategy included combinations of the keywords “breast cancer,” “targeted and systemic chemotherapy,” “Luminal A subtype,” “Luminal B subtype,” and “HER2 protein.” The review included randomized clinical trials, cohort studies, systematic reviews and clinical guidelines on the efficiency of chemotherapy for breast cancer for breast cancer in elderly women based on biological subtypes.

3. Results and Discussion

Various studies involving patients over the age of 70 with hormone-sensitive tumors have shown that Tamoxifen reduces the annual risk of breast cancer recurrence by approximately twice and the annual probability of death from breast cancer by 37%, regardless of lymph node status. Tamoxifen is well tolerated by older female patients and is affordable due to its low cost. It can also help to maintain or increase bone density and lower cholesterol levels in postmenopausal women [6]. However, there is approximately

a 1% risk of developing endometrial cancer and venous thrombosis with 5 years of use. Recommendations for annual pelvic examinations and Pap smears among elderly female patients may present certain challenges. A number of large clinical trials comparing Tamoxifen and aromatase inhibitors (AIs) were conducted, and a slight advantage in terms of recurrence rates was observed in the AI group. Nevertheless, the advantages in terms of overall survival compared with Tamoxifen are negligible. Although there are many strategies regarding endocrine therapy, the use of Tamoxifen followed by a switch to aromatase inhibitors after three years has demonstrated an approximately 1% increase in survival and represents the best strategy [6-7].

The Luminal B subtype is hormone-sensitive but more aggressive than the Luminal A subtype; it is characterized by poor differentiation, a high Ki67 proliferative index, large tumor size, lymph node involvement, and an earlier age of onset. Up to 20% of breast cancer cases occur in women over the age of 65. It has a worse prognosis and a higher likelihood of recurrence compared to Luminal A. In cases of HER2 amplification (up to 10% of tumors), the tumor may be resistant to hormone therapy, unlike targeted therapy with Trastuzumab [8-9]. In addition to possible HER2/neu overexpression, the Luminal B subtype is also characterized by a high grade of histological malignancy (G3). Endocrine therapy is the basic adjuvant treatment for elderly patients with luminal B-subtype breast cancer. The main challenge in treating elderly patients with the Luminal B subtype is determining which of them would potentially derive the greatest benefit from chemotherapy. In patients with T1 and T2 tumors and no lymph node involvement, who have hormone-sensitive tumors and are undergoing adjuvant endocrine therapy, the value of chemotherapy can be determined using prognostic tests such as Oncotype DX, MammaPrint, and others [10-11]. This analysis indicates that the greatest benefit from chemotherapy in this group is observed among patients with a high risk of recurrence, and the least benefit among patients with a low risk of recurrence, including women with 1–3 affected lymph nodes [12-14]. The authors believe that for patients with an intermediate risk of recurrence, the value of chemotherapy in reducing breast cancer mortality can be evaluated using the website www.adjuvantonline.com.

The value of chemotherapy for elderly patients with T1 and T2 tumors without lymph node involvement and low risk of recurrence is also being evaluated in randomized clinical trials. A similar study is being conducted in patients with 1–3 affected lymph nodes. The 13th International Conference on Breast Cancer in St. Gallen recommended the use of taxanes and anthracyclines for the luminal B subtype, even though it was unable to determine a preferred chemotherapy regimen [15].

The decision regarding the use of chemotherapy and Trastuzumab in elderly patients should be made on an individual basis, especially for patients who are in poor physical condition. In most cases, adding Trastuzumab to chemotherapy improved survival compared with chemotherapy alone. Elderly female patients demonstrated good tolerability of Trastuzumab, but close monitoring remains necessary. As patients get older, there is an increased risk that Trastuzumab may cause heart failure. Patients with heart disease and diabetes are at high risk for developing cardiotoxicity, and the increased risk may be due more to the prevalence of comorbidity than to age [16]. New targeted agents, such as Lapatinib and Neratinib—which have smaller molecules targeting HER2neu receptors—may also enhance therapeutic efficiency and reduce side effects when added to chemotherapy in elderly patients. The Erb-B2-overexpressing subtype is hormone-receptor-negative and is characterized by a high Ki-67 proliferation index, low differentiation, large tumor size, lymph node involvement, and a high likelihood of a poor prognosis [17]. Adjuvant Online directly compares survival rates across different chemotherapy regimens. It divides the regimens into first, second, and third (the most aggressive), based on the benefits of treatment.

The second-generation regimen, consisting of 4 cycles of TC, was found to be more effective than 4 cycles of AC; it was evaluated in a large number of elderly patients and was generally well tolerated. For patients in good physical condition who are at high risk of recurrence, treatment with a third-generation regimen improves survival by several percentage points compared with first- and second-generation regimens [18,8]. For patients with a low risk of recurrence, the authors suggest considering a second-generation regimen, such as TC, to avoid potential anthracycline-related cardiac and hematologic toxicity. For high-risk patients, a third-generation treatment regimen should be considered when there is an estimated improvement in 5-year survival of several percentage points. Third-generation regimens containing anthracyclines and taxanes should be used in patients with high functional status and minimal comorbidities.

The HER2 protein is a unique and valuable target for pharmacological treatment. It is found in 15–25% of all breast cancer cases; however, these rates are significantly lower in older age groups. Patients with HER2-positive tumors derive the greatest benefit from the combination of chemotherapy and Trastuzumab. As cardiac toxicity is the primary side effect of Trastuzumab, and the incidence of heart disease increases with age, elderly female patients are at risk of cardiac toxicity and require close monitoring. Measuring the left ventricular ejection fraction before starting therapy and every 2 months during treatment should become standard practice. The combination of Trastuzumab with Docetaxel, Carboplatin and Trastuzumab is comparable in efficiency with Trastuzumab and anthracycline-containing chemotherapy; however, it is associated with less cardiac toxicity and is strongly recommended for the treatment of elderly female patients [19].

The majority of patients with triple-negative breast cancer, compared with those with other biological subtypes, have a much earlier recurrence (usually within 5 years) and also have significantly poorer survival rates. The basal-like subtype is the most aggressive type of tumor, occurring

in approximately 15% of cases [20]. It is characterized by an earlier age of onset compared to other subtypes, poor differentiation, a high Ki-67 proliferative index, relatively large tumor size, lymph node involvement, nuclear pleomorphism, and necrosis, as well as a high likelihood of developing locally advanced and metastatic forms. A retrospective study by the Cancer and Leukemia Group B (CALGB) found that both older and younger patients experienced a similar reduction in breast cancer mortality and recurrence rates when treated with chemotherapy regimens containing a greater number of cytostatic drugs or higher doses of the agents. This large retrospective study of nearly 6,500 patients provides evidence that age should not be a barrier to intensive chemotherapy regimens if patients are in good health [20-21]. The EBCTCG meta-analysis also showed that chemotherapy was generally just as efficient in patients over 65 as it was in younger women. Chemotherapy is much more toxic than endocrine therapy and can lead to a decrease in physical activity and life quality. Palliative care without chemotherapy may be a reasonable choice for frail elderly patients [22,19]. The specific choice of chemotherapy regimen depends on several factors, including the patient's individual characteristics, the physician's judgment, the patient's preferences, and the availability of medications.

The CALGB 49907 study showed that monochemotherapy resulted in poorer outcomes in elderly patients compared with combination regimens. Two SEER retrospective studies have shown that adjuvant chemotherapy improved overall survival in elderly patients aged ≥ 70 years with a hormone -negative subtype. A prospective randomized trial conducted by CALGB found that standard CMF or AC chemotherapy was superior to Capecitabine as adjuvant chemotherapy in elderly patients aged ≥ 65 years with early-stage breast cancer [20,3]. The most significant effect was observed in the hormone-negative subtypes. Although they achieved a reduction in toxicity compared with standard therapy, recurrence-free and overall survival were higher in the standard chemotherapy group. After three phases of research involving 510 patients with stage I–III breast cancer, Jones S. et al. compared the efficiency of TC versus AC in a subgroup analysis of elderly women aged ≥ 65 and younger women. It was found that TC was associated with better recurrence-free and overall survival than AC in both age groups, including patients with hormone-negative or HER2-negative tumors [23]. Chemotherapy using the TC regimen is well tolerated with a low incidence of neutropenia (about 8%) in elderly patients. may be an option, though not in all cases [19]. These data confirm that elderly, healthy patients with triple-negative breast cancer have indications for treatment with the most advanced chemotherapy regimens.

4. Conclusions

It is very difficult to decide whether to prescribe chemotherapy to an elderly woman. This decision must be preceded by an examination of the treatment's impact on improving survival and an evaluation of its potential toxicity, which could lead to a loss of functionality and a reduced life quality.

Once the decision to prescribe chemotherapy has been made, the oncologist faces a second difficult choice: which chemotherapy regimen to select.

Sequential treatment with a single cytostatic agent may be preferable for elderly, frail patients, considering the potential reduction in the risk of toxicity.

Conflict of Interests' Statement

The authors declare no conflict of interest.

This study does not include the involvement of any budgetary, grant or other funds.

The article is published for the first time and is part of a scientific work.

ACKNOWLEDGMENTS

The authors express their gratitude to the management of the multidisciplinary clinic of Republican Specialized Scientific-Practical Medical Center of Oncology and Radiology for the supporting of our study.

REFERENCES

[1] Diab S.G. Tumor characteristics and clinical outcome of elderly women with breast cancer. / Elledge R.M, Clark G.M. // JNatlCancerInst 2000. –V. 92. – P. 550–556.

[2] Rudenstam C. Randomized trial comparing axillary clearance versus no axillary clearance inolder patients with breast cancer: first results of International Breast Cancer Study Group. Trial 10-93. / Zahrieh D. // J ClinOncol 2006. – V. 24. – P. 337–344.

[3] Schrag D. Life expectancy gains from cancer prevention strategies for women with breast cancer and BRCA1 or BRCA2 mutations. / Kuntz K, Garber J. // JAMA 2000. - V. 283. – P. 617–624.

[4] Christman K. Chemotherapy of metastatic breast cancer in the elderly. / Muss H.B, Case L.D. // ThePiedmontOncology Associationexperience. JAMA 2012. - V. 268. – P. 57–62.

[5] Slamon D. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. / Leyland-Jones B, Shak S. NEnglJMed 2001. – V. 344. - P. 783–792.

[6] Dowsett M. Prediction of risk of distant recurrence using the 21-gene recurrence score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: a TransATAC study. / Cuzick J, Wale C. // JClinOncol 2010. - V. 28. - P. 1829–1834.

[7] Semiglazov V.F. Breast Cancer: Biology, Local and Systemic Treatment. / Semiglazov V.V. // SIMK 2014. N.1. – P. 298-341.

[8] Gregor M. Trastuzumab-related cardiotoxicity among older breast cancer patients. / Zhang N, Niu J. // ASCO Meeting Abstract. JClinOncol 2012. - V. 30. – P. 135.

[9] Slamon D. Adjuvant Trastuzumab in HER2- Positive Breast Cancer. // Eiermann W, Robert N. // NEnglJMed 2011. - V. 365. - P. 1273–83.

[10] Partridge A. Adherence and persistence with oral adjuvant chemotherapy in older women with early-stage breast cancer in CALGB 49907: adherence companion study 60104. / Archer L, Kornblith A. // JClinOncol 2010. –V. 28. - P. 2418–2422.

[11] Semiglazov V.F. New approaches to the treatment of breast cancer. // Voprosy Onkologii 2013. - N. 3. - P. 288-291.

[12] Albain K. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials. / Anderson S, Arriagada R. // Lancet 2012. - V. 379. - P. 432–444.

[13] Jones S. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US oncology research trial 9735. / Holmes F, O'Shaughnessy J. // JClinOncol 2009. –V. 27. – P. 1177–1183.

[14] Wildiers H. Management of breast cancer in elderly individuals: recommendations of the International Society of Geriatric Oncology. / Kunkler I, Biganzoli L. // LancetOncol 2007. –V. 8. - P. 1101–1115.

[15] Abe O. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. / Abe R, Enomoto K. // Lancet 2005. – V. 365. – P. 1687–1717.

[16] Sawaki M. Safety of adjuvant trastuzumab for HER - 2-overexpressing elderly breast cancer patients: a multicenter cohort study. / Mukai H, Tokudome N. // Breast Cancer 2012. –V. 19. - P. 253–258.

[17] Foulkes W. Triple-negativebreastcancer. / Smith I, Reis J. // NEnglJMed 2010. - V. 363. - P. 1938–1948.

[18] Geyer C. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. / Forster J, Lindquist D. // NEngl JMed 2006. - V. 355. - P. 2733–2743.

[19] Freyer G. Adjuvant docetaxel/cyclophosphamide in breast cancer patients over the age of 70: results of an observational study. / Campone M, Peron J. // CritRevOncolHematol 2011. - V. 80. - P 466–473.

[20] Paik S. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. / Tang G, Shak S. // JClinOncol 2006. – V. 24. - P 3726–3734.

[21] Ravdin P. Computer program to assist in making decisions about adjuvant therapy for women with early breast cancer. / Siminoff L, Davis G. // JClinOncol 2001. –V. 19. – P. 980–991.

[22] Burstein H J. American Society of Clinical Oncology clinical practice guideline: update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. / Prestrud A.A, Seidenfeld J. // J Clin. Oncol 2010. - V. 28. - P. 3784–3796.

[23] Muss H. Investigators. Adjuvant chemotherapy in older women with early-stage breast cancer. / Berry D, Cirrincione C. // NEnglJMed 2010. – V. 360. – P. 2055–2065.

Copyright © 2026 The Author(s). Published by Scientific & Academic Publishing
This work is licensed under the Creative Commons Attribution International License (CC BY). http://creativecommons.org/licenses/by/4.0/