

The best treatment for older patients with breast cancer

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1. Introduction

One of the biggest risk factors for the development of breast cancer is age, and over 40% of all breast cancers diagnosed are in women aged 65 years or older [1]. Despite this, there are few standardised guidelines for the management of older breast-cancer patients, primarily due to the lack of level-I evidence and the lack of representation of older women in adjuvant therapy trials. Thus clinicians are often required to make treatment decisions for elderly patients in the face of uncertainty. This often leads to undertreatment, or less frequently, overtreatment of elderly patients, with resultant poorer outcomes.

In order to address this issue, a task force created by the International Society of Geriatric Oncology (SIOG) and the European Society of Breast Cancer Specialists (EUSOMA) has developed a set of evidence-based guidelines for the management of breast cancer in elderly individuals [2]. It is important to note that these guidelines are predominantly applicable only to elderly patients who are fit, rather than those who are less fit or frail, due to the scarcity of data relating to treatment of this latter group. Key recommendations are summarised as follows.

- For an older individual with breast cancer it is critical that all management decisions take into account physiological age, life expectancy, potential risks versus absolute benefits, treatment tolerance, patient preference and potential barriers to treatment.
- Elderly breast-cancer patient management should involve collaboration between geriatricians and oncologists. Elderly patients are at higher risk for competing comorbidities, which may not be evident on oncological assessment. Comprehensive evaluation of functional status with a multidomain geriatric assessment (CGA) is ideal, although this may not be possible in all patients. Alterna-

tively, it is reasonable to perform a functional screening assessment to identify which patients are at increased risk for functional deficits on the extended CGA. In patients in whom reversible functional deficits are detected, proactive management of these can improve quality of life and survival. Similarly, identification of interval decrease in functional status through the use of repeated geriatric assessments allows appropriate intervention and potentially improved outcomes.

2. Early breast cancer

- Surgical options for patients 70 years or older should be equivalent to those of younger patients, with age itself not an indication for less-than-standard surgical management. In some older patients it might be reasonable to omit either sentinel lymph-node biopsy or completion axillary lymph-node dissection, though this is an area of ongoing debate.
- All elderly patients undergoing breast-conserving surgery should be offered whole breast irradiation as a means to significantly reduce local relapse rates. Elderly patients with high-risk tumour (T3-4 or at least four lymph nodes involved) should be considered for post-mastectomy radiotherapy.
- Treatment of estrogen-receptor (ER) positive breast cancer with endocrine therapy alone is a suitable treatment strategy only in an elderly individual who has a limited life expectancy (less than 3 years), who is considered unfit for surgery after optimisation of medical conditions, or who refuses surgery. Geriatrician input to guide the management of comorbidities and to accurately assess life expectancy is strongly recommended.

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- Tamoxifen and aromatase inhibitors have similar efficacy in older as in younger patients and are recommended as initial adjuvant hormone therapies. The choice between tamoxifen or aromatase inhibitors should be made by balancing the slightly higher efficacy of aromatase inhibitors with the increased vulnerability of elderly patient to their toxicities. For patients who commence on tamoxifen, a switch from tamoxifen to aromatase inhibitor after 2–3 years should be considered on the basis of treatment tolerability. Similarly, for healthy elderly patients, extended endocrine therapy with an aromatase inhibitor after 5 years of tamoxifen is reasonable. In elderly patients with very low-risk tumours (pT1aN0) or severe comorbidities, the risks and toxicities of endocrine therapy may outweigh the benefits; in these circumstances it may be reasonable to omit adjuvant endocrine therapy.
- Fit elderly patients gain as much benefit as younger patients from adjuvant chemotherapy. Chemotherapy decisions should be made based on potential benefits, which are highest in node-positive, hormone-negative disease, compared with risks and toxicities. Four cycles of an anthracycline-containing regimens are usually preferred over cyclophosphamide methotrexate 5-fluorouracil (CMF). Substitution of anthracycline with taxane is also a reasonable option to reduce the risk of cardiac toxicity.
- Adjuvant trastuzumab in combination with chemotherapy should be offered to all elderly patients with HER2-positive breast cancer, without cardiac disease, and who are suitable for chemotherapy treatment. Use of single-agent trastuzumab in patients not suitable for chemotherapy might be an option, although limited outcome data are available in support of this approach.

3. Metastatic breast cancer

- Chemotherapy is indicated for ER-negative, hormone-refractory, or rapidly progressing disease.
- Single-agent chemotherapy is generally preferred, although oral combination chemotherapy is also a reasonable option in elderly patients. There is no good evidence in support of routine dose or schedule modifications in elderly patients. However, this may be appropriate in certain circumstances, based on the known toxicities and pharmacology of the chemotherapy agents coupled with comorbidities in the patient.
- All patients with human epidermal growth factor receptor 2 (HER2) positive disease should be offered HER2-targeted therapy. In fit elderly patients, anti-HER2 therapy should be given in combination with chemotherapy. Anti-HER2 therapy plus endocrine therapy is a reasonable treatment option in patients with HER2-positive ER-positive disease in whom chemotherapy is contraindicated. Similarly patients with HER2-positive ER-negative disease who are not suitable for chemotherapy may be candidates for trastuzumab monotherapy.
- While bevacizumab has demonstrated benefit in terms of improved progression-free survival in both elderly and

younger patients alike, concerns regarding both toxicities and cost efficacy make its place in elderly breast cancer management uncertain.

Increased comorbidities and polypharmacy are both more common in elderly patients. Additionally, physiological ageing can be associated with altered pharmacokinetics (drug absorption, distribution, metabolism and excretion). Each of these factors can affect the efficacy and toxicity of anti-cancer agents, making it critical that drug prescription in elderly patients be done with care. Eliminating or reducing the risk of drug interactions is best achieved with a thorough medication review before making any treatment decisions.

Poor compliance or non-compliance with oral anti-cancer medications is not uncommon in older breast-cancer patients [3–5] and can lead to reduced efficacy of therapy. It is important to consider causes of non-compliance, which may often include poor tolerability of treatment. Thus, close adverse-event monitoring and addressing specific toxicity concerns and side-effects are crucial to improve compliance, treatment tolerability and efficacy.

Older breast-cancer patients often rely more strongly on the recommendation of the cancer specialist regarding breast cancer management decisions; however, it is important to recognise that some older patients may wish to take a more active role in decision-making. While older patients are as likely to accept therapy as younger patients, they may be less willing to risk deterioration in quality of life for a potential improvement in survival [6]. For this reason, careful and clear discussions regarding diagnosis, prognosis and treatment options, as well as expectations of treatment and potential toxicities, are essential.

Conflict of interest statement

None declared

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