Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG)

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Breast cancer is increasingly prevalent in older adults and is a substantial part of routine oncology practice. However, management of breast cancer in this population is challenging because the disease is highly heterogeneous and there is insufficient evidence specific to older adults. Decision making should not be driven by age alone but should involve geriatric assessments plus careful consideration of life expectancy, competing risks of mortality, and patient preferences. A multidisciplinary taskforce, including members of the European Society of Breast Cancer Specialists and International Society of Geriatric Oncology, gathered to expand and update the previous 2012 evidence-based recommendations for the management of breast cancer in older individuals with the endorsement of the European Cancer Organisation. These guidelines were expanded to include chemotherapy toxicity prediction calculators, cultural and social considerations, surveillance imaging, genetic screening, gene expression profiles, neoadjuvant systemic treatment options, bone-modifying drugs, targeted therapies, and supportive care. Recommendations on geriatric assessment, ductal carcinoma in situ, screening, primary endocrine therapy, surgery, radiotherapy, adjuvant systemic therapy, and secondary breast cancer were updated.

Introduction

Ageing is the leading risk factor for cancer.[1,2] The prevalence of breast cancer in older adults (≥70 years) is increasing and the higher cancer mortality in older adults compared with younger women establishes a major health disparity that could be explained by advanced presentation, delayed diagnosis, organ function decline, and presence of multimorbidities.[3] Nonetheless, functional age (ie, not chronological age) and potential underlying frailty should contribute to decision making about treatment. Older patients are under-represented in clinical trials, which do not always enrol individuals who are frequently seen in routine practice. Therefore, the risks and benefits of anticancer therapy should be carefully evaluated.[4]

A multidisciplinary taskforce including specialists in medical oncology, radiation oncology, surgery, geriatrics, radiology, and epidemiology, as well as patient advocates, affiliated with the International Society of Geriatric Oncology (SIOG) was created in 2007 to prepare recommendations for the management of breast cancer in older individuals.[5] These guidelines were subsequently updated in 2012 in collaboration with the European Society of Breast Cancer Specialists.[6] In this Policy Review, we present an update of the taskforce recommendations using new evidence that has become available since 2012 (table 1). These recommendations are a consensus by an expert taskforce on available evidence and expert opinion. For extra reading on all relevant sections in this Policy Review, see appendix.

Perceptions of ageing

Frailty involves decreased physiological and functional reserve leading to susceptibility to stressors and adverse outcomes. Strayifying patients as fit, susceptible, and frail can identify those at risk of complications.[7] Collaboration between cancer specialists and geriatricians are recommended. Individuals who are frail require tailored approaches using geriatric assessments with a focus on supportive care. Similar to younger patients, fit older individuals can tolerate standard treatment. Susceptible individuals can require treatment adjustments and geriatric interventions. Competing mortality risks can justify less aggressive approaches. The National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines recommend evaluating life expectancy and calculators such as ePrognosis can assess whether cancer is likely to shorten it.[8,9] Since competing mortality risks are more prevalent in older adults, even without multimorbidities, treatment decisions should consider not only the risk of breast cancer recurrence, but also the risk of dying of other causes, which is strongly affected by frailty.

Geriatric assessment is a multidimensional evaluation aiming to determine physiological age and guide diagnostic and therapeutic interventions targeting reversible deficits and devising treatment strategies to eliminate or mitigate them.[10] Increasing evidence supports the role of geriatric assessment in the care of older patients with breast cancer. The implementation of geriatric assessment can improve tolerance, health-related quality of life, and life satisfaction.[11–15] ASCO recommends geriatric assessment for patients aged 65 years and older considered for

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	2012 recommendations by EUSOMA–SIOG	2021 recommendations by EUSOMA–SIOG
General recommendations for all aspects of management	All management decisions for an older individual with breast cancer should consider: physiological age, life expectancy, potential risks versus absolute benefits, treatment tolerance, patient preferences, and potential barriers to treatment	Screening for frailty is recommended for patients aged ≥70 years to identify those at increased susceptibility to stressors and adverse outcome (level 1); treatment can be tailored based on patients grouping as fit, susceptible or pre-frail, and frail (level 4)
Competing causes of mortality	Relative breast cancer survival is the preferred way to describe the outcome of older breast cancer patients and assessment of comorbidity and function can predict likelihood of dying from non-breast cancer causes	Even in the absence of multimorbidities, competing causes of mortality are more prevalent in older adults compared with their younger adult counterparts (level 3); treatment decisions for anticancer treatment should be based not only on risk of recurrence or breast cancer mortality, but should also weigh the risk of dying of other causes as an equally important factor (level 4)
Geriatric assessment	Collaborative geriatric and oncology management could optimise care, general health and functional status can be captured in a multidomain geriatric assessment. However, it is unclear which older patients are most likely to benefit and which tool is optimal; a screening assessment is a reasonable first step in identifying patients that could benefit from an extended CGA; active intervention for CGA-identified reversible geriatric domains can reduce morbidity and mortality and improve quality of life. Serial geriatric assessment can identify incident deterioration, for which intervention can improve outcomes	A screening tool should be considered as the gateway or minimum starting point to any cancer treatment decision making in older patients (level 3)
Chemotherapy toxicity calculators	..	Toxicity calculators (eg, CARG and CRASH) can be used to estimate the risk of grade 3–5 chemotherapy toxicity in older patients (level 3); they must not be used as the sole factor to determine whether an older patient should receive chemotherapy, but rather as an adjunct in the decision-making process (level 4)
Cultural and social considerations	..	Due to widespread immigration, society is becoming increasingly multicultural and diverse, and this should be considered in the clinical approach to patient care; older immigrants are at risk of poor outcomes due to numerous barriers to accessing care (level not applicable); engagement with a patient's social and cultural community is an important factor in improving outcomes for patients and caregivers (level not applicable)
Screening mammography	There are no strong data for screening mammography in women >70 years, screening in women aged 70–75 years could be appropriate with the ultimate decision for an individual based on risks and benefits of screening, patients' preference, physiological age and life expectancy	Biennial screening mammography in women age 70–75 years of age could benefit part of this group, but criteria to define those who really benefit are suboptimal (level 3); screening in women ≥75 years could be appropriate with the individual decision based on risks and benefits, patient preference, physiological age, and life expectancy, but might lead to increased rates of overdiagnoses (level 4)
Surveillance mammography	..	Annual or biennial surveillance mammography for breast cancer survivors ≥70 years could be appropriate, with the individual decision based on risks and benefits, tumour biology, patient preference, physiological age and life expectancy (level 4); overuse of medical services in patients ≥80 years, with advanced multimorbidities or life expectancy less than 5 years, should be avoided (level 4)
Genetic screening	..	Genetic testing might have relevant implications for families and on therapeutic decisions regardless of patient age (level 4); selection of candidates appropriate for screening should be consistent with local practice or guidelines (level 4)
Gene expression profiles	..	Integration of information regarding the general health status in multigene prognostic models is essential to ensure accuracy of these prediction tools in older patients (level 4)
Neoadjuvant systemic therapy	..	Carefully selected, fit, older patients should be considered for neoadjuvant systemic therapy similarly to younger women (level 4); less fit older patients are best served by surgery upfront that could enable systemic treatment de-escalation based on pathological findings and physical recovery after surgery (level 4); in healthy older people with high-grade, triple-negative breast cancer, optimal chemotherapy is still debated; with very limited evidence, sequential regimens with anthracyclines and taxanes can be considered in principle because of the aggressive phenotype and frequent chemosensitivity, or shorter treatment regimens (<6 months) with either alone. But the addition of platinum compounds has poor uptake in practice, even for younger patients, and is unlikely to be feasible in the large majority of older people (level 4); fit, older patients should be considered for capecitabine in case of residual triple-negative disease following neoadjuvant chemotherapy (level 4); fit, older patients should be considered for trastuzumab in case of residual HER2-positive disease following neoadjuvant systemic therapy (level 4); neoadjuvant endocrine therapy for at least 4-6 months is useful for older patients who are not immediately suitable for surgery and aromatase inhibitors are favoured over tamoxifen in view of better response rates (level 3)
Surgery	Patients ≥70 years should be offered the same surgery as younger patients; standard of care is BCS plus WBRT, or mastectomy with or without postoperative radiotherapy; mastectomy is indicated for large or multifocal tumours not amenable to conservative excision, patients who are not fit for WBRT and patients who prefer mastectomy to BCS plus WBRT; ALND is indicated for clinically positive or highly suspected nodes; in clinically node-negative disease, axillary staging by SLNB with completion ALND for tumour-positive SLNB remains the standard of care and omission of SLNB and completion ALND might be reasonable in some older patients	Surgery remains the choice of primary treatment in the majority of older patients with early breast cancer (level 1); SLNB remains the standard of care for staging the axilla in patients with clinically or radiologically negative axilla (level 3); for patients with a positive sentinel lymph node, completion axillary therapy (surgery or radiotherapy) is not always needed, and if needed, radiotherapy should be preferred to axillary clearance, especially in the cases of low axillary nodal burden and ER-positive disease requiring adjuvant endocrine therapy (level 4); axillary surgery can be omitted in patients with cT1N0 luminal A-like tumours or short life expectancy (level 4); primary endocrine therapy can be considered as an alternative in selected patients with a strongly ER-positive tumour and short life expectancy (no more than 5 years); adverse events of endocrine therapy should be considered in this decision (level 4); oncoplastic and reconstructive surgery may be offered, considering patient preferences and comorbidities (level 4)

(Table 1 continues on next page)

	2012 recommendations by EUSOMA–SIOG	2021 recommendations by EUSOMA–SIOG
(Continued from previous page)		
Primary endocrine therapy	Primary endocrine therapy should only be offered to older individuals with ER-positive tumours who have an estimated short life expectancy (<2–3 years), who are considered unfit for surgery after optimisation of medical conditions or who refuse surgery; the involvement of a geriatrician is strongly recommended to estimate life expectancy and guide management of reversible comorbidities; it is reasonable to choose tamoxifen, or an aromatase inhibitor based on potential side-effects	When primary endocrine therapy involves aromatase inhibitors, the median time to progression is approximately 5 years (level 3); the benefit of PET *vs* upfront surgery is expected to be most pronounced with a life expectancy of <5 years (level 4)
Ductal carcinoma in situ	There is no strong data available in older women with DCIS; healthy older women with localised DCIS should be considered for BCS and postoperative radiotherapy	Surgery for DCIS should consider grade and life expectancy (level 4); fit patients with high-grade DCIS should undergo surgery (level 3); in low or intermediate grade DCIS, withholding surgery or avoiding radiotherapy can be considered (level 4)
Radiotherapy	WBRT after BCS—with a boost to the tumour bed—should be considered in all older patients as it decreases risk of local relapse; there is no subgroup of healthy older patients in whom post-BCS WBRT can be systematically omitted; post-mastectomy chest wall radiation should be considered for older patients with four or more nodes or a pT3/4 tumour; hypofractionated radiation schedules offer similar local–regional control and adverse effects as standard WBRT; the evidence for PBI in older patients is not sufficiently robust to recommend it as standard therapy	WBRT remains the standard of care for most older patients following BCS and omission of radiotherapy in low-risk patients can be safe and reasonable (level 1); in patients older than 60 years, the use of a boost is advised only for those at higher risk of recurrence (level 1); PBI is recommended to women ≥50 years and grade 1–2, pN0, hormone receptor-positive, HER2-negative, tumours ≤30mm with radial margins ≥1mm (level 4) and the role of postmastectomy radiotherapy in patients with one to three positive nodes remains controversial; hypofractionated schedules (40 Gy in 15 fractions over 3 weeks, 42·5 Gy in 16 fractions over 3·5 weeks or 26 Gy in five fractions over 1 week) are recommended for older patients (level 4)
Adjuvant chemotherapy in HER2-negative disease	The decision to treat with adjuvant chemotherapy should not be age-based. Older patients with node-positive, hormone-negative disease potentially derive the largest benefit; four cycles of an anthracycline-containing regimen are usually preferred over CMF; standard doxorubicin and cyclophosphamide, and CMF chemotherapy are superior to single drug capecitabine; taxanes are associated with increased toxicity compared with younger women, but can be added to anthracyclines in high-risk healthy older patients, or replace anthracyclines to reduce the cardiac risk; patients with HER2-positive breast cancer, without cardiac disease, should be offered trastuzumab in combination with chemotherapy	The use of chemotherapy should not be guided by chronological age alone (level 4); older adults with hormone receptor-negative disease can derive most benefit from adjuvant chemotherapy irrespective of nodal status (level 3); a duration of chemotherapy beyond 3 months is an important risk factor for the occurrence of serious side-effects (level 3); standard regimens include four cycles of docetaxel–cyclophosphamide or four cycles of doxorubicin and cyclophosphamide (level 2); weekly paclitaxel (for 12 weeks) can be an option in patients unfit for polychemotherapy (level 4); only carefully selected, fit, older patients with high-risk disease (large, node-positive, triple-negative) can be considered for a sequential combination of anthracyclines and taxanes (level 4); dose-dense regimens should not be used in general based on the increased toxicity risk and the insufficient amount of efficacy data in older patients (level 4)
Multigene-expression assays	..	There is insufficient evidence about the use of multi-gene expression assays in older patients, whether for prognosis or treatment benefit prediction (level 4); integration of information regarding the general health status in multigene prognostic models is essential to ensure accuracy of these prediction tools in older patients (level 4)
Adjuvant anti-HER2 therapy	..	Adjuvant chemotherapy along with one year of trastuzumab is recommended as a standard approach in older patients with no cardiac dysfunction and early-stage, HER2-positive breast cancer ≥0·5 cm (level 2); preferred chemotherapy options include the use of taxanes without anthracyclines, for example in the form of four cycles of docetaxel–cyclophosphamide or 12 consecutive weeks of weekly paclitaxel, avoiding cardiac toxicity of anthracyclines and duration of chemotherapy beyond the 3-month threshold at risk of grade 3–5 adverse events (level 4); a sequential regimen of anthracyclines and taxanes with trastuzumab is appropriate only in a very selected group of fit, healthy older patients (level 4); pertuzumab can be added only in high risk and fit patients, but diarrhoea can be a debilitating side effect in older individuals (level 4); extended adjuvant therapy with neratinib is probably not an appropriate option for older patients because of potential risk of grade ≥3 diarrhoea (level 4); although evidence is scarce, the use of single-drug trastuzumab without chemotherapy, but with endocrine therapy if hormone sensitive, can be appropriate in susceptible and frail patients (level 4); shorter courses of anti-HER2 therapy can be considered for older patients with small, node-negative tumours or in the context of cardiac problems (level 2)
Adjuvant endocrine therapy	There is no age-dependent efficacy of tamoxifen or aromatase inhibitors; efficacy is slightly greater with aromatase inhibitors, however, older patients are more susceptible to toxicity and safety is important in choice of drug; initial treatment should be tamoxifen or an aromatase inhibitor; patients treated with tamoxifen should be considered for a switch to an aromatase inhibitor after 2–3 years; extension of adjuvant treatment with an aromatase inhibitor after 5 years of tamoxifen could be considered for healthy older patients; omission of endocrine therapy is an option for patients with a very low-risk tumour (eg, pT1aN0) or life-threatening comorbidities	The efficacy of adjuvant endocrine therapy is independent of age (level 1); good compliance should be the driving factor for treatment choice and adjusted according to side-effects (level 4); the choice of drug and decisions on its duration should be made in the context of multimorbidities and estimated risk of breast cancer recurrence as side-effects might limit compliance and impact substantially on health domains relevant to older patients (eg, myalgia, arthralgia, osteoporosis, cardiovascular risk, cognition; level 4); aromatase inhibitors are slightly more beneficial than tamoxifen with regards to risk of recurrence and breast cancer mortality and should be considered the standard of care in older women (level 4); the extended use of an aromatase inhibitor after 5 years of tamoxifen is beneficial, whereas data are less clear if they are already used as a first endocrine therapy (ie, during the first 5 years of treatment; level 1)

(Table 1 continues on next page)

	2012 recommendations by EUSOMA–SIOG	2021 recommendations by EUSOMA–SIOG
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Adjuvant bone modifying agents	..	Bone health is affected by systemic treatments for early breast cancer and its baseline assessment and monitoring are recommended in older patients (level 4); adjuvant bone modifying drugs improve bone health and can also reduce cancer recurrence risk and increase survival (level 1); adjuvant bisphosphonates (either zoledronic acid 4 mg every 6 months or clodronate 1600 mg daily) should be offered to patients with moderate-risk to high-risk disease, regardless of age (level 4); denosumab also improves bone health but provides no improvement in relapse risk and therefore should not be considered in this setting (level 2)
Chemotherapy (metastatic breast cancer)	Hormone treatment is the treatment of choice for older women with ER-positive metastatic breast cancer; chemotherapy is suggested for ER-negative, hormone refractory, or rapidly progressing disease; single drug chemotherapy and combination oral chemotherapy are feasible options in older patients; dose reductions and schedule modifications are controversial, but should be considered based on pharmacology and toxicity.	Particular care should be paid to avoiding treatment-related toxicities, this can include adjustments to treatment schedules based on pharmacological or empirical data (level 4); monotherapy is preferred over polychemotherapy regimens when possible (level 4); all available chemotherapeutics can be used in principle like in younger people, some evidence suggests the use of single drug nab-paclitaxel and eribulin in older patients (level 2)
HER2-positive disease (metastatic breast cancer)	Patients with HER2-positive disease should receive HER2-targeted therapy and chemotherapy. In patients with HER2-positive, ER-positive disease with a contraindication to chemotherapy or without life threatening disease, anti-HER2 therapy plus endocrine therapy is an option; in patients with HER2-positive, ER-negative disease, trastuzumab monotherapy could be reasonable; bevacizumab is active in older patients in terms of increased progression-free survival, however, toxicity and cost–benefit ratio are important issues that need to be further elaborated	Anti-HER2 therapy should be given unless contraindicated by impaired left ventricular ejection fraction, with treatment adjusted according to patient fitness (level 1); a taxane, preferably paclitaxel, in combination with trastuzumab and pertuzumab is recommended as first-line therapy only in fit patients, it can cause unacceptable toxicity in patients who are unfit (level 4); endocrine therapy can be suitable in lieu of chemotherapy in patients with hormone receptor-positive disease (level II); in patients who are unfit, taxane-free chemotherapy backbones include metronomic cyclophosphamide, vinorelbine or capecitabine (level 2); appropriate monitoring for diarrhoea caused by lapatinib and pertuzumab is required (level 1); trastuzumab can be used in second line or later lines of therapy in fit patients, with careful monitoring in patients who are frail (level 4)
Targeted therapies	..	CDK4/6 inhibitors in combination with endocrine therapy represent a suitable treatment in older patients, with frequent adjustments needed (level 3); endocrine therapy alone is still a reasonable first-line option in selected cases (level 3); use of everolimus should be approached with caution and on a case-by-case basis due to its worse safety profile in older patients (level 2)
Supportive care	..	Due to increased physiological vulnerability and decreased functional reserve, older patients are at risk of decompensation while receiving cancer treatment (level 4); guidelines exist for the supportive care of patients with cancer and should be followed in this cohort (level 4); for older people, a threshold for the risk of occurrence of febrile neutropenia risk lower than 20% can be used (level 4); particular care should be paid to digestive symptoms, malnutrition, pain control and depression, all of these issues may be masked by concurrent issues or present in atypical fashion (level 4); older patients are susceptible to changes in medications, side-effects, and drug interactions and as such, diligent review and monitoring of all existing medications is crucial (level 4)
Drug safety and compliance	Careful drug prescription is warranted because of physiological age-related pharmacokinetic alteration, comorbidities and polypharmacy; renal function evaluation is mandatory for treatment with renally excreted or nephrotoxic drugs; a thorough medication review is advised, ideally involving a clinical pharmacist; drug compliance should be actively promoted; close adverse event monitoring to allow prompt intervention is recommended, since older patients have lower physiological reserve, side-effects can present in an atypical fashion, and unaddressed toxicity can compromise compliance.	The risk of treatment toxicity increases with age and multimorbidity, which might affect adherence to treatment and ultimately its efficacy (level not assessed); patients with multimorbidities are at increased risk of non-adherence; non-adherence to adjuvant endocrine therapy is associated with reduced efficacy; close monitoring is recommended (level not assessed); issues relating to language barriers, cultural differences, and a lack of literacy and numeracy should be considered in the context of poor compliance or adherence (level not assessed)
Barriers to treatment	Barriers to therapy should be identified and addressed; special attention should be paid to comorbidity (particularly cognitive status, anxiety, and depression) and social setting (particularly transport) that can affect patient decisions; physician bias should not affect management; family or caregivers cannot reliably predict patient preferences, and caregiver bias should not unduly affect management	..

Level of evidence was graded according to the four-category classification proposed by the US Agency for Healthcare Research and Quality that was used by the European Society of Breast Cancer Specialists.[1] Level 1 requires at least a RCT as part of the collection of studies, with overall good quality and consistency, and support for the clinical recommendation. Level 2 requires well designed quasi-experimental clinical studies, but not any RCTs. Level 3 requires well designed descriptive studies. Level 4 requires expert judgment, particularly in the absence of good quality, relevant clinical studies. ALND=axillary lymph node dissection. BCS=breast conserving surgery. CARG=Cancer and Aging Research Group. CGA=comprehensive geriatric assessment. CMF=cyclophosphamide, methotrexate, and fluorouracil. CRASH=Chemotherapy Risk Assessment Scale for High-age. DCIS=ductal carcinoma in situ. ER=oestrogen receptor. EUSOMA=European Society of Breast Cancer Specialists. PBI=partial breast irradiation. RCT=randomised controlled trial. SIOG=International Society of Geriatric Oncology. SLNB=sentinel lymph node biopsy. WBRT=whole breast radiotherapy.

Table 1: **Summary of the EUSOMA–SIOG recommendations**

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chemotherapy.[8] Geriatric assessment can be time consuming and might not be necessary for all older patients. Several screening tools (some self-reported) can identify patients who require geriatric assessment, and should be considered as the gateway to any cancer treatment decision making in patients aged 70 and older.[16,17]

	CARG Chemo-Toxicity Calculator	CRASH tool
Patient-related factors	Age	Diastolic blood pressure; Eastern Cooperative Oncology Group performance status
Tumour-related factors	Cancer type	..
Treatment-related factors	Planned chemotherapy dose; planned number of chemotherapy drugs	Type of chemotherapy
Laboratory values	Haemoglobin concentration; creatine clearance	Lactate dehydrogenase concentration
Geriatric assessment variables	Hearing impairment; number of falls in the past 6 months; ability to take own medications; limitations in walking one block; limitations in social activities	Instrumental activities of daily living; cognitive impairment; malnutrition

CARG=Cancer and Aging Research Group. CRASH=Chemotherapy Risk Assessment Scale for High-Age Patients.

Table 2: **Variables included in the CARG and CRASH risk scores**

The Cancer and Aging Research Group (CARG) and the Chemotherapy Risk Assessment Scale for High-age patients scores estimate the risk of grade 3–5 chemotherapy toxicity in older patients (table 2) and were validated in cohorts including 20% patients with breast cancer.[18,19] The CARG Breast Cancer score has been developed and validated but is not yet available.[20] Chemotherapy toxicity calculators should be used as an adjunct in the decision making process.[21] Multimorbidity and toxicity can affect treatment efficacy (particularly endocrine therapy) as non-adherence increases with age.[22]

Cultural and social aspects, including taboos, religious beliefs, and patient values, must be considered during diagnosis and treatment, especially in the context of the current migration flows. Older adults from immigrant populations might have more disabilities, worse self-rated health, and poorer outcomes compared with the non-immigrant population. Literacy and education are also heterogeneous and some assessment tools might not be universally applicable.

Mammography screening and surveillance

Screening

Most screening programmes are extended to include people aged between 69 and 70 years and a minority until 74–75 years. The European Commission Initiative on Breast Cancer and the US Preventive Services Task Force recommend screening mammography for women aged 70–74 years despite the risk of overdiagnosis.[23,24] A meta-analysis found a relative risk reduction for breast cancer mortality of 0·80 for women aged 70–74 years,[25] although there is conflicting evidence also in younger patients. Screening every 2–3 years is deemed to provide the best balance between benefits and harms. The American Cancer Society recommends mammography in older women,[26] particularly in the context of a life expectancy of 10 years or more. However, screening is unlikely to be beneficial after age 75 years[24] and decisions should consider overall health and life expectancy.

Surveillance

No evidence supports the benefit of mammographic surveillance on disease-specific mortality for older survivors of breast cancer in the context of multimorbidities and competing mortality risks. The risk for ipsilateral recurrence and contralateral breast cancers over the age of 75 years is not defined and is affected by tumour biology and adjuvant therapy.[27] International guidelines recommend indefinite annual mammography regardless of age.[9,28] Annual or biennial mammography is recommended for women aged 70–80 years but multimorbidities, life expectancy, and frailty should be considered.[27] Annual or biennial mammography should be avoided in patients over 80 years with multimorbidities or life expectancy of less than 5 years.[29]

Genetic screening and its implications

The prevalence of pathogenic variants associated with a germline breast cancer predisposition is almost three-times less in the 65 years and older age group (5·6% *vs* 14·2%).[30] *BRCA2* and *CHEK2* mutations have been found to be relatively prevalent in women with breast cancer who are older than 65 years.[30] Nonetheless, they are less likely to undergo genetic testing, as guidelines often focus on younger populations. For older patients, genetic testing based on simple, cancer-based criteria could potentially deliver consistent, cost-effective, and patient-centred outcomes. Selection of people appropriate for screening should be considered in line with current local or national guidelines.

In the curative setting, germline pathologic variant carriers can benefit from high-risk surveillance or risk-reducing interventions in the context of an adequate life expectancy.[9] Also, carriers of genetic alterations (eg, in *BRCA1, BRCA2, PALB2, CHEK2*) should be offered cascade testing and evaluation of their relatives. For advanced disease, poly ADP-ribose polymerase inhibition is a potential alternative to chemotherapy for older people who carry *BRCA* mutations, especially regarding quality of life.[31]

Neoadjuvant systemic therapy

Fit older patients should be considered for neoadjuvant strategies similarly to their younger counterparts on the basis of the clinical subtypes of the primary tumour.[32] Because of the higher risk of adverse outcomes,[33–35] susceptible patients could be better served by upfront

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See **Online** for appendix

For **ePrognosis** see https://eprognosis.ucsf.edu

For the **CARG Chemo-Toxicity Calculator** see http://www.mycarg.org/Chemo_Toxicity_Calculator

For the **CRASH risk score tool** see https://moffitt.org/eforms/crashscoreform/

For the **CARG Breast Cancer score** see https://ascopubs.org/doi/10.1200/JCO.20.02063

surgery, particularly if the breast cancer is already operable. The likelihood of breast conservation should also be considered on the basis of disease characteristics, expected response, and patient preference. In fit older people with high-grade triple negative breast cancer, optimal chemotherapy is still debated. Similar to the adjuvant setting, sequential regimens with anthracyclines and taxanes can be considered, although there is insufficient evidence and shorter regimens remain reasonable. There are no clear guidelines on adding platinum compounds and adding these compounds can be challenging for most older adults.

Pathological response after neoadjuvant chemotherapy can guide adjuvant treatment decisions for triple-negative breast cancer and HER2-positive breast cancer.[36,37] The CREATE-X[36] and KATHERINE[37] trials enrolled few older individuals but did not show any new safety concerns. Therefore, fit older patients should be considered for such approaches in case of residual disease.

Neoadjuvant endocrine therapy is associated with lower toxicity, reasonable response rates, and similar breast-conservation rates by comparison with neoadjuvant chemotherapy, but survival data are not available. This approach can be useful in older patients who are deemed as unsuitable for upfront surgery pending preoperative assessments. Aromatase inhibitors are recommended over tamoxifen because of improved clinical and radiological response and breast conservation rates.[38] A course of 4–6 months should be considered.

Surgery

Although surgery remains the standard treatment in most older patients with early disease, there is a risk of over-treatment with competing mortality risks warranting the use of geriatric assessment and survival estimates before proceeding with it.[39] However, breast cancer surgery is generally safe, whereas endocrine therapy can cause side-effects that could potentially affect quality of life.[22]

Surgery versus endocrine therapy

Two systematic reviews show a local control and survival benefit with surgery over primary endocrine therapy in patients with a life expectancy of 5 years or more.[40,41] However, in one large cohort study,[42] no breast cancer-specific survival differences were reported between surgery and primary endocrine therapy in strong (ie, Allred score ≥6) hormone receptor-positive disease. When primary endocrine therapy involves aromatase inhibitors, the median time to progression is approximately 5 years.[42] The benefit of primary endocrine therapy versus upfront surgery is expected to be more pronounced with a life expectancy of less than 5 years.

Ductal carcinoma in-situ

Opportunistic screening in older patients could lead to potential overdiagnosis and over-treatment of ductal carcinoma in situ. Ongoing non-intervention trials will define the role of so-called watch and wait approaches. Meanwhile, fit patients with high-grade ductal carcinoma in situ and no multimorbidities should undergo surgery. In low-grade and intermediate-grade ductal carcinoma in situ, surgery or postoperative radiotherapy could be avoided based on a patient's life expectancy and competing risks.[43]

Surgery to the axilla

Less invasive approaches to the axilla in case of clinically node-negative disease are particularly relevant for older adults. Axillary clearance does not produce any survival benefit and, in older patients, regional recurrences without axillary surgery remains rare.[44] Therefore, in older adults, sentinel node biopsy should be standard for clinically or radiologically node-negative axillae. In most cases further axillary surgery can be avoided if only one or two sentinel nodes are involved[45] or replaced by radiotherapy.[46] As even sentinel node biopsy is associated with side-effects and probably does not improve prognosis by itself, omission of axillary staging can be appropriate for frail individuals with low-volume, luminal A-like tumours.

Oncoplastic and reconstructive surgery

Oncoplastic and reconstructive surgery are offered less frequently to older patients than to younger patients.[47] Some older patients decline such approaches more frequently compared with their younger counterparts, but their personal preferences should be balanced with risks. Oncoplastic and reconstructive procedures can be reasonable alternatives to simple mastectomy or breast conservation.[47] The pros and cons of complex versus simpler procedures should be carefully assessed and discussed with patients.

Radiotherapy

Radiotherapy after breast conserving surgery

Postoperative whole-breast radiotherapy halves the risk of first recurrence and remains standard of care for most older patients following breast conserving surgery.[48] However, the absolute benefit in older patients with low-grade, hormone receptor-positive disease is modest. Omission of radiotheraphy remains controversial. The CALGB 9343 trial[49] showed a locoregional recurrence rate without radiotherapy of 10%, versus 2% with radiotherapy after 12 years of follow-up in women aged over 70 years, with no detrimental effect on overall survival, and these relapses could be treated successfully by second and deferred surgery.[49] The PRIME II trial[50] showed a low risk of ipsilateral breast tumour recurrence at 5 years for those receiving whole-breast radiotherapy. Both studies[49,50] suggest omitting radiotherapy in low-risk patients can be reasonable and the results of the PRIMETIME study (International Standard Randomised Controlled Trial Number 41579286) are awaited. Recommendations regarding radiotherapy omission in low-risk patients from the NCCN were published in 2017 and National Institute for

Care and Clinical Excellence (NICE) guidelines were published in 2018 (panel).

Tumour bed boost

In the EORTC trial[51] that compared tumour bed boost versus no boost,[51] the relative risk reduction in locoregional recurrence was not statistically significant for patients aged 60 years or older. Therefore, a boost is advised in this age group only in patients with a higher risk of recurrence.

Partial breast irradiation

No trials of partial breast irradiation focused specifically on older patients. The GEC-ESTRO trial[52] of multicatheter brachytherapy versus whole-breast radiotherapy suggested that partial breast irradiation is not inferior to whole-breast radiotherapy. The UK IMPORT-LOW trial[53] showed that partial breast and reduced dose external beam radiatiotherapy is not inferior to standard whole-breast radiotherapy, with equivalent or fewer side-effects.[53] The UK consensus recommends partial breast irradiation to women aged 50 years or older or with grade 1–2, pN0, hormone receptor-positive, HER2-negative tumours smaller than 30 mm with radial margins greater than 1 mm.[54]

Regional nodal irradiation

Three randomised controlled trials[46,55,56] show the benefit of regional nodal irradiation in high-risk early breast cancer, however, no studies specifically focused on older patients. Regional nodal irradiation is indicated in patients with four or more positive nodes, but it is unclear which group of patients with one to three positive nodes benefit from it.[57]

Postmastectomy radiotherapy

There are few studies that support the role of postmastectomy radiotherapy in older women and recommendations are extrapolated from analyses done in younger patients. Postmastectomy radiotherapy is standard of care in patients with four or more positive nodes, whereas the role of postmastectomy radiotherapy in patients with three or fewer positive nodes remains controversial. A meta-analysis[48] by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed that postmastectomy radiotherapy reduced 20-year breast cancer mortality by 7·9% for patients with three or fewer positive lymph nodes and by 9·3% for patients with four or more positive lymph nodes. Therefore, some clinicians argue that postmastectomy radiotherapy should be standard for all node-positive patients, whereas other clinicians question its role in the context of current treatment approaches. Specific guidelines are available.[9,58,59] The BIG 2-04 MRC SUPREMO trial[60] evaluating postmastectomy radiotherapy in patients with three or fewer positive nodes or pN0 with lymphovascular invasion or grade 3 with no upper age limit remains in follow-up phase.[60] Although NICE and NCCN guidelines suggest that decision making should be driven by nodal disease burden,[58,61] the recommendations by ASCO, the American Society for Radiation Oncology, and the Society of Surgical Oncology highlight the relevance of age, life expectancy, multimorbidities, tumour burden, and tumour biology.[59]

Panel: **Published recommendations regarding the omission of radiotherapy post breast-conserving surgery in low-risk patients**

NCCN guidelines (2017)

- Women aged ≥70 years with invasive breast cancer, clinically node negative, who will receive adjuvant endocrine therapy (aromatase inhibitor or tamoxifen)

NICE guidelines (2018)

- A very low absolute risk of local recurrence, defined as women aged ≥65 years, T1N0, oestrogen receptor-positive, HER2-negative, and grade 1–2
- Receipt of breast-conserving surgery for invasive breast cancer with clear margins
- Commitment to take adjuvant endocrine therapy for ≥5 years

NCCN=National Comprehensive Cancer Network. NICE=National Institute for Health and Care Excellence.

Dose fractionation schedules after breast conserving surgery or mastectomy

Hypofractionated schedules are recommended for both older and younger patients as per the FAST-Forward study[62] results.

Adjuvant systemic therapy

Adjuvant chemotherapy in older adults with HER2-negative disease

Breast cancer subtype and stage are key in informing adjuvant chemotherapy decisions. Prospective trials[63] and large retrospective cohorts[64,65] confirm the potential large benefit of adjuvant chemotherapy on breast cancer-specific survival or overall survival mostly in oestrogen receptor-negative disease, irrespective of nodal status. A retrospective study showed overall survival benefit in patients aged 70 years or older with node-positive, oestrogen receptor-positive, HER2-negative breast cancer, also with comorbidities,[66] although selection bias remains a substantial limitation. For luminal disease, gene expression profiles can identify those who might benefit from chemotherapy. However, most gene expression assay validation studies excluded older patients and do not address competing risks. OncotypeDx remains the most frequently studied tool in this age group. Its prognostic accuracy is not affected by age, but a high recurrence score does not predict adjuvant chemotherapy benefit in older patients.[67] Therefore, integrating general

	Considerations
Chemotherapy in HER2-negative disease	
Regimens	
Adriamycin–cyclophosphamide × 4 cycles, CMF × 6 cycles, or docetaxel–cyclophosphamide × 4 cycles	Validated in older patients
Weekly paclitaxel × 12 cycles	Option for patients who are HER2-negative and high-risk
Sequential anthracyclines and taxanes	No data in the general older population, only to be considered for very high-risk and fit patients
Capecitabine or weekly docetaxel	No indication
Primary prophylaxis of febrile neutropenia with G-CSF	Recommended in case of polychemotherapy, even with threshold for risk of febrile neutropenia occurrence <20%
Chemotherapy and anti-HER2 therapy in HER2-positive disease	
Regimens	
TC × 4 cycles plus trastuzumab	Validated without trastuzumab in a subgroup analysis of a randomised trial, but only one single arm combination phase 2 study is available and is not specific to older adults
Weekly paclitaxel × 12 cycles plus trastuzumab	Can be considered also in high-risk patients unsuitable for polychemotherapy
TCH × 6 cycles	Not tested in older patients and probably not suitable because of high dose carboplatin
Trastuzumab without chemotherapy	Can be considered only in patients unfit for chemotherapy (plus endocrine therapy if endocrine receptor-positive)
Pertuzumab	Consider adding to trastuzumab only in high risk, node positive and fit patients if available despite scarce data on older adults are available
Primary prophylaxis of febrile neutropenia with G-CSF	Recommended in case of polychemotherapy administered every 3 weeks, even with threshold for risk of febrile neutropenia occurrence <20%
Duration	One year of anti-HER2 therapy; shorter duration possible for small pN0 tumours or if cardiac issues

AUC=area under the curve. CMF=cyclophosphamide–methotrexate–fluorouracil. G-CSF=granulocyte colony-stimulating factor. TC=docetaxel and cyclophosphamide. TCH=docetaxel–carboplatin–trastuzumab.

Table 3: **Chemotherapy regimens in HER2-negative and HER2-positive disease in the adjuvant setting**

health status with gene prognostic models is essential. Nonetheless, although results should be interpreted cautiously, this should not disqualify older patients from such tests. The ASTER 70s study (NCT01564056) will clarify the role of tumour genomic data in older patients with breast cancer.

Online prediction tools are affordable but have substantial limitations when applied to older patients.[68] NHS PREDICT is accurate in older patients only when predicting outcomes at 5 years, but not at 10 years, and is not reliable in the presence of multimorbidities and age over 80 years.[69] Additionally, it estimates survival but not the risk of recurrence. The Age Gap Decision Tool is promising in comparing local treatment with or without chemotherapy but requires prospective validation.

For the **NHS PREDICT tool** see https://breast.predict.nhs.uk/

For the **Age Gap Decision Tool** see https://agegap.shef.ac.uk/

Chemotherapy regimen choice

Although no evidence supports differential use of adjuvant chemotherapy, older adults can experience more frequent adverse events, including death.[70] Benefits of adjuvant combination chemotherapy are maintained at least until age 70, although these results were biased by chemotherapy duration[71] and limited to hormone receptor-negative and node-positive disease.[65]

Modified regimens should not be used in older patients (table 3). The CALGB 49907 trial[63] showed significantly worse survival with capecitabine versus standard regimens (four cycles of doxorubicin–cyclophosphamide or six cycles of cyclophosphamide–methotrexate–fluorouracil [CMF]) in older women, with a high interaction of oestrogen receptor status and competing risks diluting overall survival benefits with longer follow-up.[63] The ELDA trial[72] showed worse quality of life with docetaxel versus CMF and no survival benefit.

Older adults were excluded or highly selected in trials of sequential anthracycline and taxane-based regimens, which should be considered only in fit patients with large, node-positive, triple-negative tumours. Dose-dense regimens should not be used because of the increased toxicity risk and the insufficient efficacy data in older people. In many older patients, four cycles of docetaxel–cyclophosphamide might be appropriate, which is superior to doxorubicin–cyclophosphamide and more tolerable.[73] Weekly paclitaxel can be considered for high-risk patients unfit for polychemotherapy, common chemotherapy regimens that can be considered are noted (table 3).

Safety of adjuvant chemotherapy in older adults

Older patients have higher risk of chemotherapy toxicity and mortality by comparison with younger patients.[74] Risks include haematological toxicity, anthracycline-associated cardiotoxicity (occurring in up to 38%), taxane-related neurotoxicity, falls, hospitalisations, and decreased quality of life. However, functional decline and impaired quality of life might be temporary.[75] Long-term consequences include musculoskeletal events, acute myeloid leukaemia or myelodysplastic syndrome, cognitive decline, and impaired function. Chemotherapy duration (double for sequential versus single-drug

regimens) should be limited, with a 3-month threshold for increased serious side-effects.[20]

Anti-HER2 treatment in adjuvant setting

Although adjuvant trastuzumab is beneficial regardless of age,[76,77] anti-HER2 (neo)adjuvant strategies remain poorly investigated in patients age 65 years or older. Pertuzumab can be considered for high-risk individuals,[37] but diarrhoea can be debilitating in older adults, similarly with adjuvant neratinib (table 3).

SIOG recommends adjuvant chemotherapy along with one year of trastuzumab as a standard approach in older patients with normal cardiac function and early-stage, HER2-positive breast cancer larger than 0·5 cm, and consideration of pertuzumab only in selected high-risk and fit patients (table 3).[78] The preferred chemotherapy includes four cycles of docetaxel–cyclophosphamide or weekly paclitaxel. Although evidence is scarce, omission of chemotherapy and use of single-drug trastuzumab (plus endocrine therapy if needed),[79] can be appropriate in susceptible and frail patients.[78] A short course (ie, 6 months) of adjuvant anti-HER2 therapy can also be considered for older patients with small, node-negative disease or cardiac problems.

Safety of anti-HER2 therapy in older people

Age is associated with increased cardiac toxicity rates with trastuzumab,[80] with 15–40% of patients requiring early discontinuation, particularly patients who are age 80 years or older and have multimorbidities,[81] probably due to chemotherapy-related adverse events. However, up to one-third of cardiac events occur within 2 years of treatment completion, which can be more specifically related to trastuzumab.[81]

Role of adjuvant endocrine treatment

All postmenopausal women suitable for endocrine therapy should be offered it, regardless of age. However, endocrine therapy can be omitted in the absence of any documented effect on mortality in patients with very low-risk disease, short life expectancy, or both.[82]

Choice of drug

Selection of drugs should consider multimorbidities and recurrence risk. Aromatase inhibitors result in slightly better reduction in recurrence and breast cancer-specific mortality compared with tamoxifen, and are preferable upfront, especially in high-risk patients.[83] Following a few years of aromatase inhibitors, switching to tamoxifen is similarly effective to their continuation. Musculoskeletal side-effects can impair adherence to aromatase inhibitors; long-term problems include osteoporosis, cardiovascular risk, diabetes, hypercholesterolaemia, and cognitive impairment. Conversely, aromatase inhibitors are associated with a lower risk of venous thrombosis, endometrial cancer, and fatty liver disease compared with tamoxifen. Good compliance should drive treatment decisions.

Duration of therapy

Letrozole improves survival outcomes versus placebo among patients who receive an initial 5-year course of tamoxifen. After 5 intial years of aromatase inhibitors, data are less clear compared with the evidence supporting the use of endocrine therapy for 5 years alone (and not 10 years): a recurrence-free survival benefit is not confirmed in all studies, although bone-related adverse events are more frequent. The modest effect on recurrence-free survival and the effect on bone health is confirmed by large meta-analyses. Therefore, the current standard of care should include 5 years of endocrine therapy, and extended therapy can be offered to fit, healthy older women who are at high risk of disease recurrence who tolerated the first 5 years.[84] In patients who are frail, recommendations should be guided by the individual circumstances.

Role of adjuvant bone modifying drugs

Adjuvant systemic therapies for breast cancer are associated with an increased risk of bone loss. Therefore, a baseline assessment of bone mineral density in older patients suitable for adjuvant endocrine therapy is mandatory, followed by calcium and vitamin D supplementation, and use of bisphosphonates to preserve bone mass while on aromatase inhibitors. Also, adjuvant bisphosphonates also improve survival outcomes in patients with early-stage disease.[85] An EBCTCG meta-analysis[86] documented a 2–3% benefit in breast cancer mortality limited to postmenopausal women receiving bisphosphonates.

Zoledronate or clodronate should be offered regardless of age to postmenopausal women with moderate to high-risk breast cancer according to international consensus. Evidence is insufficient for alendronate and risedronate. Bisphosponate use should take into account the minor improvement in long-term survival and their potential side-effects, including electrolyte disturbances (mostly hypocalcaemia), atypical fractures and osteonecrosis of the jaw,[87,88] multimorbidities, renal function, fitness, and patient preferences. Evidence on the role of denosumab is conflicting and denosumab should not be considered in the adjuvant setting for older patients to reduce mortality. The ABCSG-18 study[89] showed improved disease-free survival and bone fracture rate in patients on adjuvant denosumab but the subsequent D-CARE study[90] did not detect any benefit in bone metastasis-free survival or disease-free survival. Additionally, a rebound effect with more vertebral fractures occurring upon its discontinuation has been shown.

Systemic treatment for metastatic disease

Different treatment schedules, dose reductions, or stepwise dose-escalation before reaching standard

Search strategy and selection criteria

Each taskforce expert did a scoping literature review on PubMed on individual topics pertaining to breast oncology (MeSH: "older" or "elderly" and "breast cancer" and "surgery", "radiotherapy" or "systemic therapy") and any updates available since the previous recommendations were published in April, 2012. The list of topics included epidemiology, geriatric assessment, cultural and social considerations, genetic screening, ductal carcinoma in situ, screening, surveillance imaging, primary endocrine therapy, surgery, radiotherapy, adjuvant and neoadjuvant systemic therapy,gene expression profiles, treatment of secondary breast cancer, chemotherapy toxicity prediction, bone-modifying drugs, targeted therapies and supportive care. The experts presented the results of each individual scoping review to the taskforce during various meetings held between February, 2019, and August, 2020. During these meetings, the need to update the previous recommendations was discussed and consensus reached by unanimity; the level (ie, amount and quality) of evidence was graded according to the four-category classification proposed by the US Agency for Healthcare Research and Quality and, in 2002, was used by European Society of Breast Cancer Specialists.[1]

recommended dose might be required in older patients[91] and reduce the risk of adverse outcomes.

Chemotherapy

Chemotherapy should be considered in suitable older patients with hormone receptor-negative disease, hormone receptor-positive disease resistant to endocrine therapy or with rapidly progressive disease, or extensive visceral involvement, and based on geriatric assessment and patient preferences. The increased toxicity risk in this age group mandates particular attention to minimising side-effects.[8] Single-drug regimens are preferred over poly-chemotherapy[6] and chemotherapy toxicity prediction tools can also be useful. Preference should be given to drugs that have been studied in older populations. Nab-paclitaxel is associated with very few allergic reactions, does not require steroids, and is safe and effective in patients older than 65 years.[92] After receiving anthracyclines or taxanes, eribulin is also appropriate, with similar efficacy and toxicity regardless of age and no effect on geriatric assessment parameters or quality of life.[93]

For **ESMO guidance** see https://www.esmo.org/

For **MASC guidance** see https://www.mascc.org

For **SIOG guidance** see https://www.siog.org/

HER2-positive metastatic breast cancer

Older patients with HER2-positive metastatic breast cancer and adquate cardiac function should receive HER2-directed therapy on the basis of their fitness.[78] Although docetaxel or paclitaxel in combination with trastuzumab and pertuzumab are recommended in fit patients, taxanes can cause severe toxicities. In older patients not suitable for taxanes, capecitabine or vinorelbine can be considered. The EORTC 75111-10114 study[94] enrolling older patients evaluated trastuzumab and pertuzumab with or without metronomic oral cyclophosphamide. Vinorelbine along with dual anti-HER2 blockade can also be considered.

Endocrine therapy with trastuzumab plus pertuzumab or lapatinib is a reasonable alternative for patients with oestrogen receptor-positive disease, although diarrhoea can be an issue that needs close monitoring. Trastuzumab emtansine (T-DM1) is recommended in later therapy lines in fit older patients, but further research in frail patients is warranted.

Targeted therapies in luminal tumours

Efficacy of cyclin-dependent kinase 4/6 (CDK4/6) inhibition is age independent in the subgroup and pooled analyses of landmark studies of palbociclib, ribociclib, and abemaciclib,[95–98] with no age-related changes in pharmacokinetics. Nevertheless, patients age 75 years or older experience higher rates of toxicity and dose modifications.[98] Although endocrine therapy alone is still reasonable in particular patients, CDK4/6 inhibitors are a suitable treatment in older patients.[99]

Everolimus should be used with caution in older patients in view of its safety profile. A subgroup analysis of the BOLERO-2 study[100] revealed a higher rate of discontinuations in patients age 70 years or older and more on-treatment deaths. 26% of patients enrolled in the expanded access BALLET trial[101] were aged older than 70 years, which similarly reported more frequent adverse event-related dose discontinuations, reductions, and interruptions.

Supportive care

Supportive care is important because cancer and its treatment can lead to various degrees of decompensation of older patients. Detailed guidance by the European Society for Medical Oncology, the Multinational Association of Supportive Care in Cancer, and SIOG for supportive care for older adults is available.

Digestive symptoms

Nausea and vomiting can be treatment related or have alternative causes. In older individuals, diagnosis can be challenging as clinical signs might be absent or atypical. Guidelines for prevention of chemotherapy and radiation therapy-induced nausea and vomiting should be followed.[102] General management guidelines for diarrhoea, constipation, and stomatitis are available.[103–105]

Malnutrition

More than 30% of older patients have severe malnutrition in hospital and nursing home settings. Malnutrition can lead to osteopenia and osteoporosis, sarcopenia, and immunological deficiencies, and iron, vitamin B12, or folate-related anaemia, and predicts survival outcomes at 3 years. This can be improved by implementing timely interventions (eg, replacing nutritional deficits).

Depression

Depression in older cancer patients is often under-recognised and untreated, but it can be successfully managed with psychological support and, when suitable, antidepressants. Drug interactions should be considered, such as those between selective serotonin-reuptake inhibitors and tamoxifen.

Pain control

Pain can be related to or complicated by multimorbidities such as arthritis or osteoporotic fractures. Older patients are generally susceptible to changes in drug doses, side-effects, and drug interactions. Particular attention should be paid to potential side-effects of non-steroidal anti-inflammatory drugs (eg, effect on renal function or development of gastric ulcers). Guidelines are available[106,107] but the caveats must be considered.

Febrile neutropenia prevention and treatment

Guidelines on the primary prophylactic use of white blood cell growth factors[108] acknowledge the increased risk of myelosuppression in individuals age 65 years or older. In the general population, the febrile neutropenia risk threshold of 20% or higher is for consideration of primary prophylaxis, but for older people, a lower threshold (>10%) can be used, which is reached in older persons when using standard myelosuppressive regimens as anthracyclines or docetaxel–cyclophosphamide.

Conclusions

The management of breast cancer in older adults should consider the intrinsic heterogeneity of this population and involve routine use of geriatric assessments and close interaction with members of the multidisciplinary team. In the context of the limited applicability of the evidence generated in younger or more fit individuals, patient preferences, life expectancy, predicted survival benefits, and effect on anticancer therapy toxicity and quality of life should be carefully considered in decision making.

Contributors

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