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REVIEW ARTICLE

Change of paradigm in treating elderly with breast cancer: are we undertreating elderly patients?

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Abstract

Developed countries face significant population ageing in the near future. Within 20 years, the average age will approach 50 years and the largest population cohort will be those over 65 years. The incidence of breast cancer increases with age, with a risk in women of 0.44% by the age of 30, 3.82% by the age of 70 and 10% by the age of 80. Breast cancer is responsible for one out of every three cancer-related deaths. Elderly patients have higher mortality rates and most breast cancer-related deaths are observed in women over 65. There appears to be a trend that elderly patients with breast cancer receive less than the standard treatment compared to younger counterparts and this leads to poorer outcomes. The rationale for treating elderly breast cancer patients more conservatively is that breast cancers in this cohort are more commonly oestrogen receptor (ER) positive which gives the clinician the option to treat with hormonal manipulation alone. In addition, elderly patients present at a later stage compared to younger patients who frequently present with early (stages I and II) breast cancer. This review aims to give an overview of the diagnosis, treatment options and surveillance of breast cancer in elderly women (over 75 years) and to discuss the change in perception of the term 'elderly' and the reasons for undertreatment in the elderly patients.

Keywords Assessment · Breast cancer · Elderly · Treatment

Introduction

Developed countries face significant population ageing in the near future. Within 20 years, the average age will approach 50 years and the largest population cohort will be those over 65 years [1]. The incidence of breast cancer increases with age, with a risk in women of 0.44% by the age of 30, 3.82% by the age of 70 and 10% by the age of 80. Breast cancer is responsible for one out of every three cancer-related deaths [2]. Elderly patients have higher mortality rates and most breast cancer-related deaths are observed in women over 65 [3].

There is no strict medical definition of the term 'elderly' with some studies referring to those older than 65 years, while others use a definition of over 70 or even 80 years. This has created confusion in medical field especially when certain treatments are given to the so-called elderly population which are not evidence based. Furthermore, there is no doubt that sometimes we come across patients with a chronological age of over 70 or even 80 but biologically better than a 50 years old. This will further limit the definition for the term elderly which we should not rely on neither in treatment nor in trial involvement.

There appears to be a trend that elderly patients with breast cancer receive less than the standard treatment compared to younger counterparts and this leads to poorer outcomes [4]. The rationale for treating elderly breast cancer patients more conservatively is that breast cancers in this cohort are more commonly oestrogen receptor (ER) positive which gives the

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clinician the option to treat with hormonal manipulation alone. In addition, elderly patients present at a later stage compared to younger patients who frequently present with early (stages I and II) breast cancer [5].

This review aims to give an overview of the diagnosis, treatment options and surveillance of breast cancer in elderly women (over 75 years) and to discuss the change in perception of the term 'elderly' and the reasons for undertreatment in the elderly patients.

Diagnosis of breast cancer in elderly

The recent extension of the age for breast screening from 65 to 69 in many countries has led to a change in the definition of elderly patients to those over 70 years as these are not included in a screening programme [6]. Therefore, diagnosis of breast cancer in this group is usually through a symptomatic breast clinic or as an incidental finding while investigating for another illness.

A patient's biological age can be quite different from their chronological age; hence, a general assessment as described below should be performed before any decision regarding the treatment in an elderly patient.

Assessment

Initial assessment is an important aspect when dealing with an elderly patient with breast cancer. It is crucial to determine their functional status and comorbidities. Furthermore, it is quite vital to assess the quality of life in any elderly patient with breast cancer prior to starting any treatment modality and this should be thoroughly looked at both in clinic and in MDT (multidisciplinary team meeting).

Clinicians are in no doubt that the survival of any patient undergoing treatment will be impacted by the physical function which includes the ability to bathe, shop, walk several blocks and push or pull an object [7]. Those with an excellent function have a low mortality in comparison to those with a high degree of functional loss in whom 2-year overall survival is low. Furthermore, we need to determine the real risk to the patient which might not be the 5 mm DCIS but rather their dementia, hypertension or ischaemic heart disease. A comprehensive geriatric assessment is crucial in assessing this group of patients and to optimise treatment outcome and survival [8]. Mohile et al. [8] commented on this in their review and they stated that it is vital for oncologist to have all the information on the physiologic and functional capacity in this cohort of patients in order to give a safe and effective treatment. This can be achieved through a Comprehensive Geriatric Assessment.

It is often difficult to choose the best treatment for an elderly breast cancer patient when anaesthesia and surgery may be hazardous, radiation might not help and chemotherapy could be more harmful.

Refinement of decision-making in the elderly patients

ePrognosis

This is an online repository of published geriatric prognostic indices for community dwelling, nursing home or hospitalised patients. Calculations are based on patient demographics, comorbidities including smoking, in addition to baseline activity level. The assessment is via the ability to walk a quarter of a mile alone or assisted, the number of hospitalisations in the past year, the ability to manage money, being able to bath and shower and pulling or pushing large objects. In calculating life expectancy, it can be used to inform adjuvant therapy decisions [9].

Today, the presence of ePrognosis Cancer Screening App for iphones and ipads helps further the use of this tool. This decision aid uses prognostic information about older adults to help clinicians and older adults decide if investigating cancer is likely to be more beneficial or harmful. The app assesses patient age, gender, body mass index, symptoms and functional impairment to calculate a mortality risk to help determine if a patient is likely to live > 5–10 years.

ePrognosis not only helps regarding the suitability of the patient for surgical treatment but also helps in determining the post-hospital mortality index [10]. It is quite valuable to estimate the life expectancy from non-breast cancer causes before making treatment decisions in older patients.

Charlson Index

The Charlson Comorbidity Index contains 19 categories of comorbidity and predicts the 10-year mortality for a patient who may have a range of comorbid conditions. It is quite useful in assessing patient with breast cancer before and after surgery and to evaluate the association of comorbidities on breast cancer survivors' quality of life [11]. Each condition is assigned a score of 1, 2, 3 or 6 depending on the risk of dying associated with this

condition. For a physician, it is helpful to know how aggressive one should be in patient management. Higher scores indicating greater comorbidity (patients with a score > 5 have essentially a very high risk of dying at 1 year). For example, a patient may have cancer, but also heart disease and diabetes such that the costs and risks of the treatment outweigh the short-term benefit from treatment of the cancer [12].

Quality of life

There are tools in assessing quality of life in older populations. Some of these tools are for general population, others for cancer patients in elderly patients. One of such tools is known as Older People's Quality of Life Questionnaire (OPQOL-35) [13] and the brief version of this tool (OPQOL-Brief) is quite a useful tool in elderly patient's assessment. This new "brief" version was developed by asking older people to prioritise the most important items from the OPQOL-35. Instead of the 35 questions in the original one of OPQOL, the brief version comprises of 13 questions and it was found to be quite reliable and valid assessment of quality of life in older age.

The effect of health on quality of life is both variable and subjective. There are multiple dimensions in health-related quality of life which include the presence of physical symptoms that distressing to the elderly patient such as pain, nausea and constipation. Furthermore, emotional status, functional activities, social activities and interpersonal relationships are all considered here.

Tools for adjuvant treatment in elderly

Predict PREDICT tool [14] is designed to give a prediction for 5- and 10-year survival with and without adjuvant therapy and the benefit of adding hormone therapy. This tool involves data on the patient's age, mode of detection of the breast cancer (screen detected, symptomatic and unknown), tumour size, tumour grade, number of positive lymph nodes, the presence of micro-metastases, receptor status, Ki67 and chemotherapy regimen. PREDICT can make a very good estimate how any one woman may respond to additional treatment.

Nomogram MD Anderson Cancer Centre has a Breast Cancer Nomogram to predict the additional benefit of radiation for older patients with breast cancer treated with conservative surgery [15]. It contains data on age, race, tumour size (> or < 2 cm), ER status and nodal status. Lymph node status is categorised into three options: clinically assessed node-negative, pathologically confirmed node-negative and pathologically confirmed node-positive. The calculation will estimate the risk of mastectomy over 5 and 10 years with and without radiotherapy.

Adjuvant online This is another tool that determines the benefit of adjuvant therapy in breast cancer patients [16]. It will estimate the 10-year survival for patients in addition to any benefit from chemotherapy. Different treatment options can be estimated, from surgery alone to adding hormonal manipulation or chemotherapy or any combination.

Deficit accumulation frailty index Mandleblatt et al. looked at patients 65–91 years old and examined whether a deficit accumulation frailty index predicted long-term mortality [17]. They found that most of the patients (76.6%) were robust and could consider chemotherapy if indicated. Patients who are frail or pre-frail have elevated long-term all-cause and breast cancer mortality and they concluded that frailty indices could be useful for treatment decision-making and care planning with older patients.

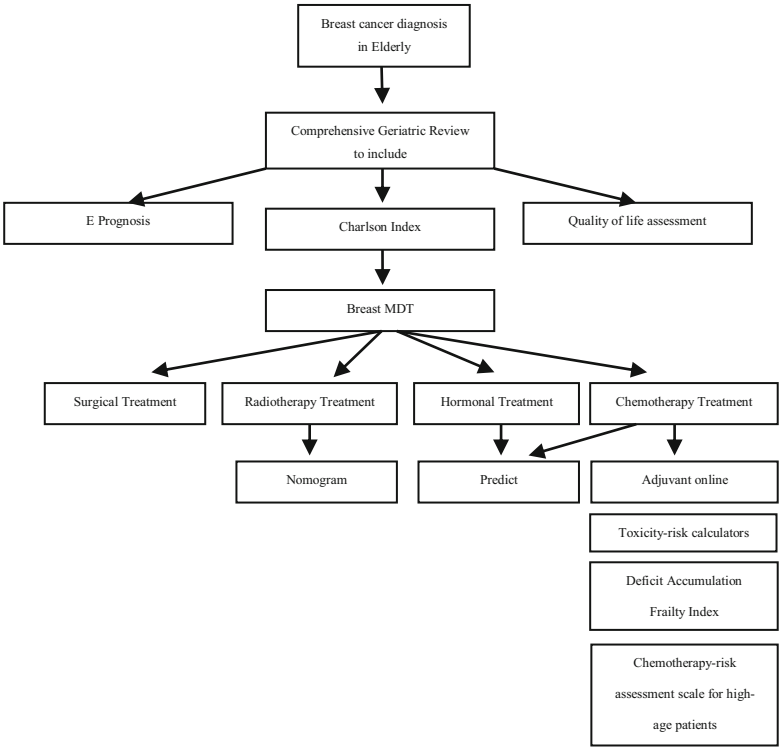
Toxicity-risk calculators This is a toxicity predictive model which has been validated and was shown to be quite useful prior to chemotherapy treatment for older patients with cancer [18]. This calculator includes gender, age, weight, height, serum creatinine, haemoglobin level, cancer type, the dose of chemotherapy treatment and if a single agent or combination chemotherapy to be used as well as six variables attained via a short geriatric assessment which includes hearing status, number of falls, hearing problems, ability to take medications, ability to walk one block and social activities limitations due to health or emotional problems. From the result, a risk score can be calculated and applied accordingly.

Chemotherapy risk assessment scale for high-age patients This tool integrates both chemotherapy and patients risk for older patients [19] to estimate the risk of severe toxicity based on the specific chemotherapy regimen, diastolic blood pressure, instrumental activities of daily living, lactate dehydrogenase, performance status, mini-mental status and a mini-nutritional assessment.

In summary, it is quite clear the decision-making in treating an elderly breast cancer patient is quite complex; however, there are many tools to assist us in that decision

and all these should be brought to MDTs prior to the final discussion with the patient and family members.

An MDT flow chart can be a useful tool in assessing these patients as outlined below.



Imaging in the elderly

Mammography

Mammography remains the most common imaging modality in diagnosing breast cancer in the elderly population [20] and it remains the gold standard method to detect early-stage breast cancer before lesions become clinically palpable. Mammography is very good in detecting ductal carcinoma in situ (DCIS) and calcifications. Although in screening groups mammography has helped to decrease the mortality rate by 25–30% when compared with a control group after 5 to 7 years [21], these results cannot be extrapolated for elderly patients as there are not enough data in this age group.

Tomosynthesis

Advancement in digital mammography led to 3D mammography or so-called tomosynthesis. Braithwaite et al. [22] recently published in clinical interventions in ageing journal regarding the new imaging modalities and concluded that the new imaging technologies impact on screening mammography outcomes in older women is not well understood and the use of routine screening with two-dimensional (2D) digital mammography is the primary means of early breast cancer detection; however, the use of newer imaging technologies, such as digital breast tomosynthesis (DBT, also referred to as 3D mammography), is diffusing rapidly into clinical practice.

Ultrasonography

Ultrasound is another adjunct in detecting breast cancer in elderly patients both in patients with palpable and impalpable breast abnormalities. There are very high false positive and false negative rates [23] with ultrasound; thus, it is suggested that sonography alone should not be used in elderly assessment [24] but should always be used with mammography or other imaging techniques. Adding ultrasound to mammogram screening has added benefit but at the expense of an increase false positive rate [25]. As elderly patients' breasts are less dense than younger patients, mammography remains the main imaging modality; however, it is important to consider ultrasound in evaluating dense breast. 3D and automated

ultrasound has shown some promise to reduce operator dependant factor and to give a better imaging modaity [26].

Magnetic resonance imaging

Magnetic resonance imaging (MRI) is not widely used in breast cancer diagnosis in the elderly population. Melissa et al. [27] published in Breast Journal the use of MRI in the elderly and they concluded that the greatest benefit of MRI are in women presenting with an occult primary cancer and there is minimal additional benefit in elderly patients with breast cancer undergoing MRI imaging for extent of disease evaluation or in follow-up.

Computed tomography

Computed tomography (CT) scan is generally used in staging process in elderly patients with breast cancer rather than a diagnostic tool. Nowadays, breast incidentalomas are seen more often due to increasing use of CT in a variety of diagnostic pathways. In a systematic review by Bach et al. [28], they looked at ways to distinguish between benign and malignant features and they concluded that benign and malignant breast incidentalomas are not safely distinguished from each other on standard CT and they advocated that all breast incidentalomas should be evaluated by further radiological and or histological investigations.

Bone scan and positron emission tomography

Recent advancement in technology and the availability of new imaging modalities have led to some imaging techniques to be replaced by others. Bone scan is one of the most common and oldest examinations among all nuclear medicine procedures. Bone scan is used in evaluation of benign bone disease and metastatic disease from the breast in elderly patients. Though the reported sensitivity of bone scan is high, its specificity is low due to increased metabolic activity seen in benign disease such as trauma, infection, inflammation and degenerative joint diseases. In cases of widespread involvement, metastatic disease should be sought. A single focal lesion is almost always a cause of dilemma in reporting and further imaging such as a single-photon emission computed tomography (SPECT), a SPECT/computed tomography (CT) or a correlative CT or magnetic resonance imaging (MRI) can help. Bone scanning is part of staging investigation following a diagnosis of breast cancer; however, with the availability of positron emission tomography (PET) scanning, more and more people opt for PET rather than bone scan. A recent publication in *British Journal of Cancer* [29] by De placid and co highlighted the move from bone scan to PET scan and they concluded that there is no evidence that the delivery of new tests to asymptomatic patients improves breast cancer outcome. Bone scan in elderly patients with suspected fracture in a weight bearing bone should be further investigated in the absence of osteoporosis to out-rule bonny metastasis from breast cancer.

Some other modalities such as molecular breast imaging (MBI), scintimammography and single-photon emission computed tomography (SPECT) are generally used as an adjunct in breast cancer detection and staging especially in women with dense breasts and less in elderly patients.

Biopsy and subtyping

Biopsy remains the cornerstone in triple assessment breast investigation for elderly patients which includes clinical breast examination, radiological imaging and breast biopsy.

Breast cancer subtypes

The majority of elderly breast cancer patients (65–78%) are oestrogen receptor (ER) positive, progesterone receptor (PR) positive, human epidermal growth factor (HER2) receptor negative and have a low Ki-67 or so called Luminal A breast cancer that respond well to hormonal manipulation. The second group are known as Luminal B which is defined as ER positive, PR negative and HER2 either positive or negative. Luminal B (HER2 negative) has ER positive, HER2 negative and either Ki-67 high or PR low; Luminal B-like (HER2 positive) has ER positive, HER2 over-expressed or amplified, any Ki-67, and any PR. Patients from this group are likely to benefit from chemotherapy and may benefit from hormone therapy and treatment targeted to HER2.

The third group is known as HER2 positive group which includes tumours that are ER negative and PR negative, but HER2 positive. HER2 breast cancers are likely to benefit from chemotherapy and treatment targeted to HER2. The fourth group is known basal-like and also known as triple-negative breast cancer, which accounts for around 15% of patients and they are negative to ER, PR and HER2 receptors.

Ki-67 Index

A higher Ki-67 index has been found to correlate significantly with young age, large tumours, positive lymph nodes, negative ER/PR, p53 over-expression and positive HER2 in comparison to older populations. A higher Ki-67 index has also been found to correlate with a poorer prognosis and early recurrence (< 2 years). On the other hand, a lower Ki-67 index has correlated with a favourable prognosis and late recurrence (> 10 years). Thus, proliferative activity as determined by Ki-67 may reflect the aggressive behaviour of breast cancer and predict the time of recurrence and the appropriate therapy required in treatment. It is therefore important to take the Ki-67 index into consideration in the treatment and follow-up of breast cancer patients.

Serum tumour biomarkers

Ca 15.3, Ca 27-29 and CEA (carcino-embryonic antigen) are used as breast biomarkers but with a low sensitivity and specificity in elderly patients and not reliable in breast cancer detection although can be helpful in metastatic settings.

Treatment

The European Registration of Cancer Care (EURECCA) study 3, a large-scale international comparison of the treatment of elderly patients with non-metastatic breast cancer, showed that there are substantial differences in the use of surgery, hormone therapy and chemotherapy between European countries [30]. They concluded the reason for this is due to the lack of evidence for the treatment of older patients with breast cancer.

Surgery

A Cochrane meta-analysis by Fennessy et al. [31] concluded that omitting primary surgery in unselected elderly women with operable breast cancer who were fit for the procedure resulted in an increased rate of progression, therapeutic intervention and mortality. Furthermore, primary hormonal treatment with tamoxifen is inferior to surgery (with or without hormonal therapy) in terms of local control and progression-free survival in medically fit older women and does not result in significantly better overall survival. Surgery to the breast may consist of mastectomy or alternatively breast-conserving surgery followed by radiotherapy. In rare cases, radiotherapy may be required after mastectomy. Axillary surgery may consist of sentinel lymph node biopsy or axillary lymph node dissection and sometimes followed by radiation therapy accordingly. Breast surgery is low risk even among elderly patients; however, it is the comorbidities that can increase complications with this group of patients [32]. However, there are still a lot of discrepancies in treating elderly patients with breast cancer and many centres opt for hormonal treatment as the first line treatment without any consideration to the other available modalities. This has led to operative treatment being limited to less than half of the elderly population. When surgical treatment is employed, it is most likely to be breast only without axillary surgery [33]. Martelli et al. [34] showed in their publication that there was no benefit in axillary surgery in elderly patients with early breast cancer and clinically negative nodes in terms of breast cancer mortality from immediate axillary dissection. They went further and stated that even sentinel node biopsy could also be foregone due to the very low cumulative incidence of axillary disease in this age group. Their final conclusion was that axillary dissection should be restricted to the small number of patients who later develop overt axillary disease. Furthermore, Boughey [35] et al. stated in their publication that may be the time has come to stop surgical staging of the axilla altogether in woman over 70 years of age with hormone receptor positive; however, in their final conclusion, they recommend further research to be performed for proper individualization of SLN surgery for women age 70 years or older with hormone receptor positive disease before it is eliminated altogether.

Adjuvant treatment

The aim of adjuvant treatment is to increase the chances of cure and reduce the risk of recurrence. Undertreating a patient of any age is associated with poorer outcomes. There is up to a 20% improvement in distant disease-free survival with adjuvant therapy [36]. The risk of recurrence is same for older patients in comparison to younger patients. The life expectancy of an older patient is a key factor in determining adjuvant management and if deemed healthy enough they should receive the same treatment as a younger population.

Hormonal treatment

Hormonal treatment is generally based on the EORTC 10851 trial [37]. This trial compared tamoxifen alone with modified radical mastectomy in patients aged 70 years or older. The EORTC 10851 trial showed that hormonal treatment results in faster disease progression compared to surgical treatment. However, there was no difference in the overall survival between the two treatments. These results have led to breast surgery being performed only in 38% patients with locally or regionally limited cancer who received their first treatment. Surgical treatment was performed considerably less often in elderly patients than younger cohort in other studies. According to data from the Dutch Cancer Registry, there is a sharp decline in guideline adherence for unselected women aged 80 years and older with primary operable breast cancer, with an observed shift from appropriate locoregional treatment toward endocrine therapy [38].

Most elderly breast cancer patients are hormone receptor positive; therefore, hormonal treatment with Tamoxifen has traditionally been the most common treatment option for ER-positive, HER2-negative disease. Irrespective of age, the use of Tamoxifen for 5 years has shown to reduce the annual recurrence by 39% and breast cancer mortality rate by 31% [39]. Aromatase inhibitors (AI) have shown to further reduce this risk by an average of 4% in post-menopausal patients [40]. It is important to consider the side effects of Tamoxifen including deep vein thrombosis and uterine cancer. AIs do not have these side effects; however, some of the associated side effects are fatigue, nausea, depression, arthralgia/myalgia and vaginal dryness.

A randomised controlled trail by Johnston et al. [41] reported that combining Tamoxifen with surgery in fit breast cancer patient older than 70 years showed no advantage in the rate of regional recurrence, metastasis or survival, even though local control was improved.

An area that is still under debate is the addition of chemotherapy to endocrine therapy in hormone receptor-positive patients and chemotherapy alone in hormone receptor-negative patients. Studies have shown that the benefit of poly-chemotherapy progressively decreases with increasing age [39]. In patients younger than 50, there is a reduction in the annual recurrence rate by 35% and mortality rate by 30%; however, this reduction is only 23 and 9% respectively for the older age group. The benefit of chemotherapy remained in patients over 70. Overall, chemotherapy appears to mostly benefit ER-negative patients who are either node positive or node negative [39, 42]. Muss et al. reported a similar improvement in relapse-free and overall survival in patients both younger and older than 65 years for node-positive disease; however, the older age group have a higher rate of treatment related mortality [43].

In cases of metastatic breast cancer in elderly patients, Palmeri et al. [44] showed that hormone therapy is the first line and once resistance develops, chemotherapy can be an option, although data is lacking to support this.

Radiation therapy

Patients who have breast-conserving surgery will have adjuvant radiotherapy to the breast to reduce the risk of local recurrence [45]. There are fewer indications for adjuvant radiotherapy following mastectomy. Radiotherapy to axilla has an important role to play especially after the Z0011 [46] trial which compared axillary node dissection to no dissection in node-positive patients. Darby et al. [47] reported that radiotherapy after surgery not only halved the risk of local or distant 10-year recurrence but also reduces breast cancer annual death rate in early-stage breast cancer patients stages I and II by a sixth.

Recently, a systematic review and a meta-analysis by Chesney et al. [48] showed the superiority of combining radiotherapy with Tamoxifen to Tamoxifen alone. They concluded that in patients older than 70 years, radiotherapy reduces the risk of breast and axillary recurrence, but does not impact distant recurrence or overall survival in early-stage breast cancer treated with breast-conserving surgery and Tamoxifen.

Radiotherapy should be offered to patients with high risk of local recurrence which includes women with tumours larger than 5 cm, those with locally advanced tumours, with surgical margins near the tumour, and those with more than four positive axillary lymph nodes irrespective of the operative procedure performed. Intra-operative radiotherapy has also been investigated and Vaidya et al. [49] recently published a large randomised controlled trial comparing a targeted intraoperative radiotherapy (TARGIT) to conventional postoperative radiotherapy after breast-conserving surgery for women with early-stage breast cancer. They reported that in breast cancer patients older than 45 years with hormone-sensitive invasive ductal carcinoma up to 3.5 cm in size, TARGIT concurrent with lumpectomy within a risk-adapted approach is as effective as, safer than and less expensive than postoperative radiotherapy.

Other roles for radiotherapy include locally advanced breast cancer, fungating or ulcerating cancers and there is also a significant role in metastatic breast cancer.

Adjuvant radiation use in older women with early-stage breast cancer at Johns Hopkins was published recently by Pollock et al. [50]. They found that factors associated with higher radiation therapy omission rates included older age and not having pathological nodal evaluation. The radiation therapy omission rate did not vary by race, tumour type, grade or size. Their conclusion was that the implementation of the National Comprehensive Cancer Network guidelines has not been reliably followed at their institution and suggested that other tools should be considered to apply the guidelines more consistently.

Chemotherapy

Patients with ER-negative breast cancer are not candidates for hormonal treatment and may therefore require chemotherapy. Patients with hormone-positive cancer but with negative prognostic markers such as HER2 over-expression, positive lymph nodes and a high proliferation rate should also be considered for chemotherapy. A French study on the use of chemotherapy in elderly [51] showed that women aged 75–80 years received chemotherapy over four times less often than women aged 65–74 years. They concluded that chronological age remains a barrier to receive chemotherapy for older breast cancer women but the establishment of a formal collaboration between oncologists and geriatricians seems to be an effective way to improve care delivery in this population.

Oncotype DX

Oncotype DX is a valuable tool to determine the benefit of adjuvant chemotherapy in oestrogen receptor positive breast cancer. Oncotype has revolutionised the use of chemotherapy and age should not be a factor in ordering Oncotype test. Swain et al. showed that in patients with ER-positive breast cancer, age alone does not reflect the underlying individual tumour biology, and concluding that the Recurrence Score result may add potentially useful information for personalised treatment decisions. Furthermore, results from a large Danish observational study presented at the European Society for

Medical Oncology (ESMO) annual meeting showed disparate outcomes in breast cancer-specific mortality between patients 70 years or greater and those under 70. The study included 207,320 eligible patients with node-negative, ER-positive breast cancer diagnosed between 2004 and 2011. The results showed that mortality was higher in patients over 70 who were either not tested with Oncotype DX, or had a recurrence score result greater than 18. These data are contrary to the general perception that older women tend to have only low-risk disease and reinforce the value of examining tumour biology with Oncotype DX in older women to predict recurrence score and aid in adjuvant treatment decision-making. Patients aged 70 or older were also less likely to receive chemotherapy, supporting continued examination of the issue of undertreatment of the elderly.

Triple-negative breast cancer

A meta-analysis by Clarke et al. [52] and Early Breast Cancer Trials Collaborative Group looked at relapse-free and overall survival in a large cohort, the majority (70–80%) of whom were likely triple negative. Those patients aged 50–69 years, about 60% of whom were node positive, there was a 6% absolute lower risk for dying as a result of breast cancer with the use of older chemotherapy regimens alone, and by more aggressive therapies, including new treatments, these results will continue to improve. These findings confirm that older, healthy patients with triple-negative breast cancer should be considered for treatment with state-of-the-art chemotherapy.

In an unplanned subset analysis, the researchers confirmed that the greatest therapeutic benefit in these older patients was in those with triple-negative breast cancer. Overall, there was a marked improvement in patients with triple-negative breast cancer that favoured standard chemotherapy, which underscores the value of chemotherapy in older patients with the triple-negative phenotype.

Recently, Kaplan et al. [53] published a retrospective cohort study of triple-negative breast cancer patients and they found that most elderly patient did not receive chemotherapy. However, survival appears to be equivalent in older and younger patients despite less aggressive treatment in patients 75 years and older but did not comment on the disease-free survival.

HER2-positive breast cancer

All trials have shown a substantial benefit in adding trastuzumab to chemotherapy in treating older patients with HER2-positive breast cancer. The Breast Cancer International Research Group (BCIRG) 006 [54] study showed that older patients can do well with non-anthracycline chemotherapy that includes trastuzumab. This was an important therapeutic option in older patients, because trastuzumab-related cardiotoxicity is age related, and older people as a group are more likely to have trastuzumab-related toxicity.

Locally advanced breast cancer in elderly patients

This is quite challenging in treating elderly patients with locally advanced breast cancer. A recent publication by Hornova et al. [55] looked at 80 patients aged 70 to 96 years diagnosed with locally advanced breast cancer with the majority (66%) having at least one significant comorbidity. The median overall survival was 50.6 months and hormonal therapy was the dominant mode of systemic treatment. They concluded that elderly patients with locally advance breast cancer have a poor prognosis. Age and serious comorbidities were negative prognostic factors.

Metastatic breast cancer

A recent review by Cabarrou et al. [56] looking at phase II clinical trials in metastatic elderly breast cancer concluded that a phase III clinical trial will be challenging; furthermore, they stated that it is crucial to evaluate new therapies (targeted therapies, immunotherapies) using adequate methodologies.

Conclusion

There is no doubt that as life expectancy is increasing, elderly patients require a new approach in treating their breast cancer. Undertreatment of elderly breast cancer patients has risks when it is based on chronological age alone and hormonal manipulation alone might lead to treatment resistance. Therefore, any elderly breast cancer patient should have a proper assessment and all the treatment options available should be offered to the patients accordingly unless there are contraindications. A case by case treatment in this age group would be more appropriate depending on patient's assessment, comorbidities and wishes. Furthermore, elderly patients should be considered for clinical trials as they have been very under represented thus far [57]. These trials are important to analyse treatment and response in this age group and to improve treatment modalities for these patients. On the other hand, we need to ensure that we do not expose elderly frail patients to the side effects of treatments particularly chemotherapy if risks outweigh any survival benefit. Multidisciplinary meetings should now incorporate tools such as ePrognosis and Charlson index in decision-making to maximise survival benefit for these patients. In the meantime, there should be a change in paradigm in elderly patients with breast cancer so that undertreatment is minimised and maximum survival is achieved.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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