Original Article

Practical consensus recommendations regarding the management of hormone receptor positive early breast cancer in elderly women

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Abstract

Breast cancer is a leading cause of death among women, and its incidence increases with age. Currently the treatment of breast cancer in older patients is almost identical to their younger counterparts. This expert group used data from published literature, practical experience and opinion of a large group of academic oncologists to arrive at these practical consensus recommendations for the benefit of community oncologists regarding the management of early breast cancer specifically in elderly women.

Key words: Axillary node, biomarkers, breast conservation surgery, Ki67, radiotherapy

Introduction

In India, we are now witnessing more and more number of patients being diagnosed with breast cancer in the younger age groups. Still, 22% of the patients diagnosed with breast cancer are in the age group of above 60 years.[1,2] The primary treatments for early breast cancer are surgery, adjuvant radiotherapy and adjuvant systemic therapy. The purpose of this manuscript is to help the community oncologist optimise the management of early breast cancer in the elderly.

Expert oncologists from all over India met to discuss and reach a consensus statement to provide community oncologists practical guidelines on the management of early breast cancer in elderly women. The discussion was based on published evidence and practical experience in real life management of such patients. The expert group discussions were moderated by Dr Govind Babu. The core expert group consisted of Dr Ashish Goel, Dr Sandeep Agarwal, Dr Sachin Gupta, Dr Piyush Kumar, Dr B.K Smruti and Dr Vineeta Goel. Members of the panel were also allowed to share their personal experiences and make comments. This manuscript is the outcome of the expert group discussion and consensus arrived at in 2017.

Defining Clinical Cohort and Practice of Expert Group Panel Members

The primary objective was to provide a consensus statement for community oncologists that could be applicable as ready-to-use practical recommendations. Hence, the applicable setting was outlined by defining the clinical cohort and current practice of the participating delegates and expert group panel members – on the basis of which this document was prepared. The experts discussed a case of a 75 years old normotensive, non-diabetic fit woman who developed a 2.8 cm lump in OUQ left breast with clinically non palpable axillary lymph nodes. Trucut biopsy showed invasive duct carcinoma, ER/PR 80% positive and Her 2 neu negative. Metastatic workup came out to be negative. Based on this case, a series of questions were put up for poll upon which the expert group discussed and aimed to reach a consensus. Each question had multiple choice options from which participants were to select the one most appropriate for their clinical practice setting. The expert group then formed the practical consensus recommendations for the community oncologists.

Treatment - Surgery

When asked which surgery they would recommend, a total of 71.3% polled oncologists were in support of recommending BCS with sentinel lymph node dissection [Table 1]. The experts recommended that breast conservation surgery (BCS) with sentinel lymph node dissection is to be offered as standard of care for all patients irrespective of age and that the physiological age of the patient, rather than the chronological age should be considered while planning treatment in elderly patients. The experts added that the management of breast cancer in older women is not different to that in younger patients. There are no standard guidelines set for older patients, and the management is different from one country to another and from one centre to another. An international study comparing local treatments (surgery and radiotherapy) for operable breast cancer in older women showed that in many countries, most patients had undergone conservative surgery.[3] Two randomized controlled trials[4,5] showed better locoregional control in favour of the surgical group as compared to the tamoxifen group. The panelists concluded that BCS with sentinel node dissection should be offered as the standard of care in elderly patients. The group also added that it is possible to avoid axillary dissection in women aged 60 or older with hormone receptor positive early breast cancer and clinically node negative disease, provided that the patients receive endocrine therapy following surgery.[6] While some studies have shown longer survival for patients undergoing axillary dissection,[7] others have failed to show any benefit.[8]

Treatment - Radiotherapy

In women with early breast cancer undergoing BCS, radiation treatment to the preserved breast is standard practice.[9]

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Majority of the polled oncologists (71.3%) were in support of recommending radiation therapy to elderly patients [Table 2]. In older women, it has been suggested that whole-breast radiation given per guidelines following surgery decreases in-breast recurrences and lengthens disease-specific and overall survival as well.[10-13] A study by Truong *et al.*[14] enrolled 4,836 patients aged 50–89 with early stage breast cancer who were treated with BCS. After a median follow-up of 7.5 years, radiation omission was associated with significantly increased relapse rates as well as poorer disease-specific and all-cause survival. However, the expert panel noted that survival benefits usually are not noted until 5 to 10 years after diagnosis, which makes such a treatment of marginal or no benefit in those with life expectancies lesser than 5 years.[15] The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) published an updated analysis using individual patient data from 10,801 patients included in 17 randomized trials of radiation after breast-conserving surgery.[16] This publication revealed that the addition of radiation therapy was associated with a highly significant absolute benefit of 15.7% in any first recurrence (local, regional, or distant recurrence) at 10 years. The expert panel concluded that radiation therapy should be offered to elderly patients, especially to those with longer life expectancies.

Treatment – Chemotherapy

To the question whether they would recommend chemotherapy, a total of 50% of the polled oncologists gave a negative answer. Thirty percent of the polled oncologists were in support of recommending chemotherapy while the remaining 20% opined that they will opt to go for more tests on biopsy before proceeding further [Table 3]. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis, which included 3,700 women, confirmed that tamoxifen reduced the relapse rate by 28% and mortality by 21% in women aged 70 years or more.[17] The experts concluded that hormonal therapy should be offered to all older patients with hormone receptor positive breast cancer.[18-20] The expert panel suggested that adjuvant chemotherapy has been shown to be consistently beneficial only for younger patients.[21-23] Studies have also suggested that adjuvant chemotherapy is most beneficial for patients over 65 years of age when their tumor is estrogen receptor negative or positive lymph nodes.[24-26] Considering the available evidence, the expert panel consensus was that chemotherapy in patients older than 70 years of age should be offered when the tumour is hormone receptor negative.

Molecular Tests Required for Decision Making

To the final question as to what other tests would they recommend in case the patient is unable to afford Oncotype Dx, a total of 50% of the polled oncologist were in favour of recommending Ki67 testing. Additional 30% of the polled oncologists were in support of recommending Prosigna test while the remaining 20% voted testing for the grade of tumour [Table 4]. Ki-67 protein expression plays an important role in predicting the proliferative status of tumour cells and deciding the future course of therapy in breast cancer.[27] Its potential uses include prognosis, prediction of relative responsiveness or resistance to chemotherapy or endocrine therapy and as a dynamic biomarker of treatment efficacy

Table 1: Question 1 - What is your advice to the patient regarding surgery?

Options	BCS with sentinel lymph node dissection	BCS with axillary nodes dissection	Modified radical mastectomy	Any other
Percentage of polled oncologists	71.4	0	28.6	0

Expert group consensus: BCS with sentinel lymph node dissection should be offered as standard of care for all patients irrespective of age. Axillary node dissection is not always necessary. BCS=Breast conservation surgery

Table 2: Question 2 - What is your advice to the patient regarding radiotherapy?

Options	Yes	No
Percentage of polled oncologists	71.4	28.6

Expert group consensus: Radiation therapy should be offered to elderly patients, especially when the life expectancy is more than 5 years

Table 3: Question 3 - What is your opinion on giving chemotherapy?

Options	Yes	No	Will do more tests before deciding
Percentage of polled oncologists	30	50	20

Expert group consensus: Chemotherapy in patients older than 70 years of age should be offered when the tumour is hormone receptor negative. Hormonal therapy may be considered in older patients with hormone receptor positive breast cancer

Table 4: Question 4 - What tests will you do if patient is unable to afford oncotype?

Options	Ki67	Grade of tumour	Prosigna
Percentage of polled oncologists	50	30	20

Expert group consensus: Ki67 bio-marker testing and Prosigna assay are useful predictive and prognostic markers and should be used as appropriate

in samples taken before, during, and after neoadjuvant therapy.[28]

It is known that breast cancer is truly heterogeneous disease.[29,30] Late relapses occur even after 20 years. Significant percent of elderly women with breast cancer still die of their cancer as opposed to age. Aggressiveness of disease needs to be matched with aggressiveness of the health-care programme implemented. Low risk patients should be spared unnecessary prescriptions. Multi-gene signature assays are now proven to be of prognostic and predictive significance.[31,32] Although the largest data is available with Oncotype Dx, there are a few limitations such as cost, lack of data in Indian patients, change in cut off score and applicability only in subset of patients. Hence, a search for additional biomarkers is ongoing. Some possibilities are Ki67, PAM50, and Mammaprint. The focus for this discussion was Ki67 and PAM50. A meta-analysis by de Azambuja *et al.*[33] evaluated 46 studies including 12155 patients who were considered to present positive tumours for the expression of Ki-67 according to the cut-off points defined by the authors. The analysis found that Ki-67 positivity was associated with higher probability of relapse in all patients. Furthermore, Ki-67 positivity was also associated with worse survival in all patients. Some studies have demonstrated a reduction in Ki-67 index after chemotherapy,[34-37] tamoxifen therapy,[38,39] and chemo-endocrine therapy.[40,41]

The expert panel concluded that significant evidence exists to justify the use of Ki67 testing to help decision making.

Looking at the evidence on the prognostic and predictive accuracy of the PAM50-based Prosigna breast cancer gene signature assay, the expert panel deemed it worth considering as well.[42-46] Some studies have also shown that PAM50 provides a better estimate of prognosis and of prediction of treatment benefit than IHC-based surrogates.[42-44] The expert panel concluded that Ki67 bio-marker testing and Prosigna assay, both are worth considering in helping predictive and prognostic decision making.

Take Home Message

1. Breast conservation surgery (BCS) with sentinel lymph node dissection should be offered as standard of care for all patients irrespective of age. The physiological age of the patient, rather than the chronological age should be considered while planning therapy in elderly patients. Axillary node dissection is not always necessary.
2. Radiation therapy should be offered to elderly patients, especially when the life expectancy is more than 5 years.
3. Chemotherapy in patients older than 70 years of age should be offered when their tumour is hormone receptor negative. Hormonal therapy may be considered in older patients with hormone receptor positive breast cancer.
4. Ki67 bio-marker testing and Prosigna assay are useful predictive and prognostic markers and should be used as appropriate.

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Conflicts of interest

There are no conflicts of interest.

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