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Management of primary metastatic breast cancer in elderly patients—An international comparison of oncogeriatric versus standard care

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ABSTRACT

Background: An oncogeriatric approach may affect management of elderly patients with breast cancer. However, little is known about oncogeriatric care in the metastatic setting. Therefore, we performed an international comparison of management of elderly patients with primary metastatic disease who were treated in two different care settings.

Materials and Methods: Patients who were ≥70 years at diagnosis of primary metastatic disease were eligible. The first cohort comprised a population-based cohort of 104 patients (Comprehensive Cancer Center West, The Netherlands), who all received standard care. The second cohort comprised a hospital-based cohort of 42 patients (H. Lee Moffitt Cancer Center, Florida, United States), who all received oncogeriatric care.

Results: No large differences in patient and tumor characteristics were observed between both cohorts. Most patients in the standard care cohort received systemic therapy as primary therapy, whereas most patients in the oncogeriatric cohort received a combination of systemic and local therapy. Patients in the standard care cohort received fewer lines of treatment (mean number of treatments 2.1 vs. 3.6, $p < 0.001$), and particularly received less breast surgery, chemotherapy, and trastuzumab. Three-year overall mortality was 71% (95% CI: 61–83%) as compared to 58% (95% CI: 42–75%) among patients in the oncogeriatric care cohort (multivariable HR: 1.59 [95% CI: 0.88–2.87], $p = 0.125$).

Conclusions: In primary metastatic breast cancer, oncogeriatric care intensifies treatment and might improve survival in elderly patients. Future studies on a larger scale should investigate the potential for improved survival, and whether this is accompanied by a better (preservation of) quality of life and functional status.

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1. Introduction

Over 40% of all patients with breast cancer are 65 years or older at diagnosis,[1] and this proportion is expected to further increase due to increasing life expectancy.[2] Despite representing a large proportion of patients with breast cancer, the elderly are frequently under-accrued in clinical trials,[3] and therefore breast cancer management in older women is limited by a lack of level 1 evidence.[4] Consequently, older patients are at risk for both under- and overtreatment.

A collaborative geriatric and oncology management can optimize care in elderly patients.[4,5] An oncogeriatric approach leads to greater attention being paid to comorbidity and geriatric issues, which may result in better selection of adequate treatment on an individual basis, prevention of complications, and a lower risk of patient deconditioning. Previously it has been shown that use of a comprehensive geriatric assessment may result in changes in treatment strategy.[6] Through these mechanisms, an oncogeriatric approach may improve patient outcomes.

However, little is known about such an oncogeriatric approach in elderly patients with metastatic breast cancer.[7] Older women are more likely to present with more advanced disease as compared to younger patients[4]; 16.3% of patients aged 65 years and older present with distant metastases, versus 10.5% in patients younger than 65 years.[2] Therefore, we performed an international comparison of treatment and outcome of elderly patients with primary metastatic breast cancer who were treated in a standard care setting as compared to those who were treated in an oncogeriatric care setting.

2. Methods

2.1. Cohorts

The study flowchart is shown in Fig. 1. Two patient cohorts were constructed. Cohort 1 comprised a population-based cohort of elderly patients with breast cancer treated in the Comprehensive Cancer Center West in The Netherlands, who all received standard care (*standard care cohort*). Patients were identified from the Dutch Cancer Registry. Cohort 2 comprised a hospital-based cohort of elderly patients treated at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, United States (US). All patients received oncogeriatric care (*oncogeriatric care cohort*). Patients were identified from the Moffitt Cancer Registry and the Total Cancer Care program.

All women with primary metastatic breast cancer, who were 70 years or older at diagnosis, and were diagnosed between January 1st 2008 and December 31th 2011 were eligible. To increase the power of the analysis, inclusion in the oncogeriatric care cohort was extended to January 1st 2003. Patients with a history of breast cancer less than 5 years prior to diagnosis of metastatic breast cancer were excluded, as these were considered to have recurrent disease. By means of chart review, data were collected on tumor, patient and treatment characteristics. For the oncogeriatric care cohort, vital status and date of last follow-up were established directly from the patient's medical record or through linkage of the Moffitt Cancer Registry data with the National Death Index. Patients who moved out of the region were censored at time of last follow-up visit. For the standard care cohort, vital status and date of last follow-up were established either directly from the patient's medical record or through linkage of cancer registry data with municipal population registries, which record information on vital status. Cohort follow-up censoring date was July 1st 2012.

2.2. Description of Care

In the standard care cohort, no structured oncogeriatric approach was present. Irrespective of age at diagnosis, patients were discussed in multidisciplinary meetings, and treatment was based on national guidelines. By contrast, in the oncogeriatric care cohort a structured oncogeriatric approach was provided for all patients. Patients were seen in the Senior Adult Oncology Program and underwent a geriatric screening at first visit to evaluate functional status, mood and cognition, nutritional status, and quality of life.[6,8] Any adverse finding prompted further evaluation and possible interventions.[6] All patients were discussed in a multidisciplinary meeting with a focus on geriatric parameters. Moreover, risk scores were used to predict benefit and toxicity from systemic therapy in order to personalize treatment.[9]

2.3. Statistical Analyses

SPSS version 20.0 (SPSS, Chicago, Illinois, USA) was used for statistical analyses. Continuous data were presented as mean (standard deviation, SD). Differences in patient and tumor characteristics between the cohorts were analyzed by means of Pearson's $\chi 2$ test or the Fisher Exact test in the event of low numbers in any cell.

As the majority of patients with metastatic breast cancer die from breast cancer, the primary outcome of interest was overall mortality. A Cox proportional hazards model was used to assess the influence of care setting on overall mortality, with results reported as hazard ratio (HR) with 95% confidence interval (CI). Covariates were included in the multivariable model if they were judged to be clinically relevant, and comprised age (continuous) and the year of diagnosis (continuous). All statistical tests were two-sided. A p value of <0.05 was considered statistically significant.

2.4. Instrumental Variable

Differences in overall mortality were evaluated by means of cohort as an instrumental variable. An instrumental variable can be used as a substitute for randomization in non-randomized studies, and may reduce confounding by indication under the assumptions that the instrumental variable is associated with the exposure, unrelated to the confounders and has no direct association with the outcome other than through exposure.[10,11] Thus, cohort membership was used as an instrumental variable, as a surrogate for type of care. The two geographically distinct cohorts represent different settings of care. The place of residence determines a patient's allocation to the cohort and thereby determines the probability of being treated in a standard or in an oncogeriatric care setting. The interpretation of the results strongly depends on