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Prognostic value of geriatric assessment in older patients with advanced breast cancer receiving chemotherapy

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ABSTRACT

Introduction: The prognostic value of geriatric assessment in older patients with breast cancer treated with chemotherapy is largely unknown.
Methods: Fifty-five patients with advanced breast cancer aged 70 years or older were assessed by Mini Nutritional Assessment (MNA), Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), Groningen Frailty Indicator (GFI) and Mini Mental State Examination (MMSE). Levels of albumin, hemoglobin, creatinine and lactate dehydrogenase were measured. Patients completing at least four cycles of chemotherapy were reassessed by GFI and MMSE and mortality was evaluated using Cox regression analysis.
Results: The mean age was 76 year (SD 4.8). Inferior MNA and GFI scores were associated with increased hazard ratios for mortality: 3.05 (95% confidence interval [CI]: 1.44–6.45; $p = 0.004$) and 3.40 (95% CI: 1.62–7.10; $p = 0.001$), respectively. Physical aspects of frailty worsened during the course of chemotherapy. Laboratory values were not associated with assessment scores nor were they predictive for mortality.
Conclusions: Malnutrition and frailty, rather than cognitive impairment and laboratory values, were associated with an increased mortality risk in these elderly breast cancer patients with advanced breast cancer.

1. Introduction

In developed countries, breast cancer accounts for nearly one third of all new cases of cancer in women.[1] Older age is an important risk factor for breast cancer. More than 40% of breast cancer diagnoses and nearly 60% of breast cancer deaths occur in women aged 65 years or older.[1] Because older cancer patients are hardly represented in randomized clinical trials of chemotherapy, the results of these studies cannot predict for outcomes and toxicities of treatment in this population. Therefore, population based studies should address outcome- and treatment modifying factors in older patients to provide future methods to distinguish older patients who are likely to benefit from treatment from those who are not.

A comprehensive geriatric assessment (CGA) can be used to systematically assess health and functional status in older people.[2–4] A CGA may disclose the existence of geriatric syndromes, such as frailty and cognitive dysfunction not previously recognized by the treating physician. Several studies use the concept of frailty as a hallmark of geriatric syndromes, in accordance with Balducci's algorithm for the management of elderly cancer patients.[5–7] It has previously been shown that psychosocial deficits and comorbidity are associated with poor treatment tolerance and mortality, independent of age and stage of disease.[8] Also, cognition deficits and frailty predict for toxicity and early treatment withdrawal in

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patients treated with chemotherapy.[9,10] Furthermore, malnutrition has been identified as a predictor of increased mortality.[11,12]

The impact of cognitive dysfunction on tolerance of chemotherapy and mortality is largely unknown. The main focus of research on cancer treatment and its cognitive side effects have concentrated on adjuvant treatment in breast cancer patients.[13] A recently published meta-analysis showed that cognitive deficits after chemotherapy in breast cancer patients are small in magnitude and limited to the domains of verbal and visiospatial ability[14] and in an accompanying editorial the suggestion was made that the effect of chemotherapy on cognition is underestimated and that more research is needed.[15]

Anemia, hypoalbuminemia and renal dysfunction were identified by others as risk factors for frailty and chemotherapy toxicity.[16,17] For example, anemia is a powerful prognostic factor for the development of frailty related problems such as muscle weakness, reduced performance, falls, and mortality.[18–20] It is interesting to know if laboratory measurements are more predictive for the number of chemotherapy cycles and mortality than GA.

We performed a GA that provided combined information on several domains of health and function in older patients: cognition, nutritional status, comorbidity, functional-, and psychosocial status. For practical reasons we decided to use a limited set of questionnaires and tests instead of a complete CGA. We considered this as an effective method to capture a broad spectrum of data and at the same time minimizing resources and time spent by health care providers. Such a cost effective choice might broaden the reach of such assessments.[10,21] Furthermore, laboratory values of serum albumin, creatinine, lactate dehydrogenase (LDH) and hemoglobin were measured.

With this variant of an abbreviated GA and selected laboratory tests we studied outcome modifying factors in older breast cancer patients treated with chemotherapy. In patients who completed at least four cycles of chemotherapy GFI and MMSE were repeated in order to examine the effect of chemotherapy on these parameters of frailty and cognition.

2. Patients and methods

2.1. Study design

This clinical cohort study involved patients aged 70 years or older ($n = 55$) with advanced breast cancer for whom chemotherapy was prescribed by their medical oncologist. Patients were recruited between May 2004 and February 2010 from the outpatient oncology practices of three general and one university hospital. Participating hospitals were situated in the western part of the Netherlands: Reinier de Graaf Groep in Delft, Groene Hart Hospital in Gouda, HAGA hospital in The Hague and the Leiden University Medical Center. Participation of these hospitals started at different time points because of time needed for training of dedicated nurses in the technique of GA.

During the study period all patients aged 70 years or older for whom a treatment plan was made that involved chemotherapy were prospectively assessed by trained nurse practitioners using the following tests: Mini Nutritional Assessment (MNA),[22] Groningen Frailty Indicator (GFI),[23] Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE),[24] and Mini Mental State Examination (MMSE).[25] If possible, the IQCODE was filled in by family or caregivers. These validated tests were selected to assess in the elderly patients the important domains of mobility, physical fitness, polypharmacy, psychosocial resources, cognition, weight loss and nutrition, striving for a minimum of overlap between the domains. Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) were not separately assessed as GFI is considered to screen for dependency. Given the fact that many older patients have a time limited span of attention, we considered 45 min the timelimit per interview. For patients completing at least four cycles of chemotherapy, assessment by GFI and MMSE was repeated at the end of chemotherapy or at six months after start of chemotherapy.

Patients received treatment according to standard of care, therefore, ethical approval and consent were not considered necessary to be obtained. Patients with brain metastases were excluded.

For this paper, we selected all women with advanced breast cancer from a larger cohort of patients treated with chemotherapy for a variety of cancers. A part of this cohort has been previously described.[26] A flow diagram of the study is given in Fig. 1.

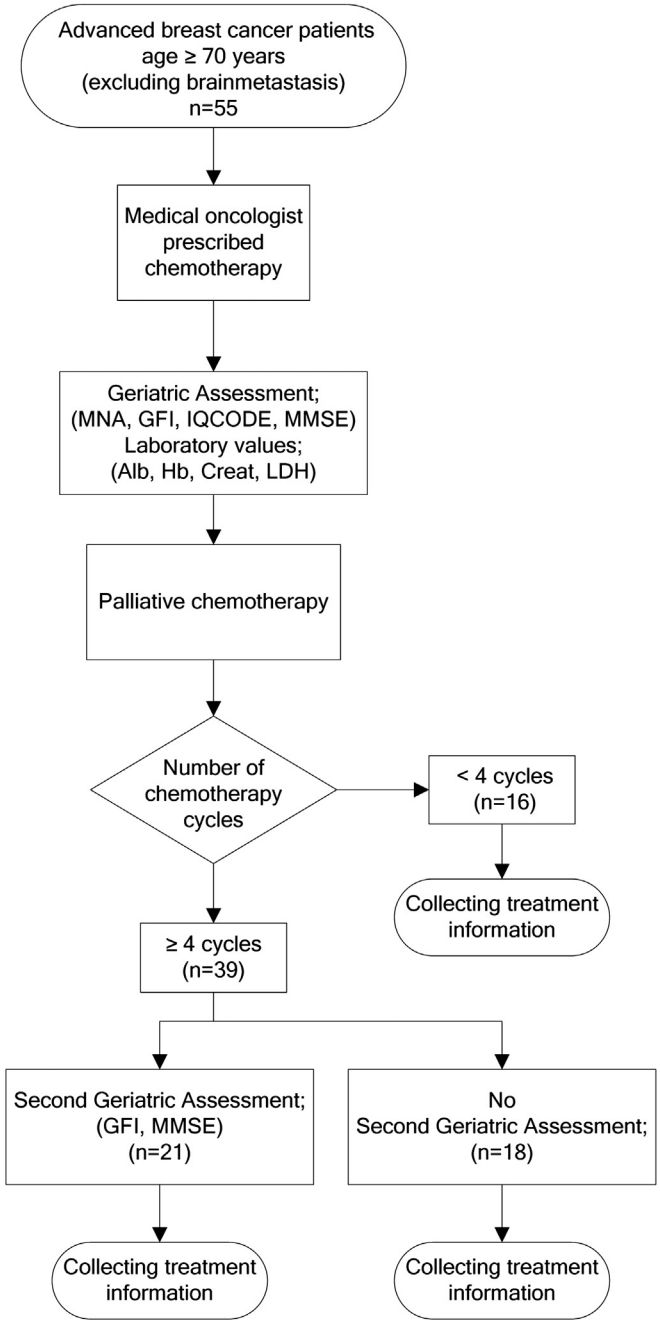

Fig. 1. Flow diagram of the study.