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Functional status decline in older patients with breast and colorectal cancer after cancer treatment: A prospective cohort study

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ABSTRACT

Objectives: The aim of the present study was to disentangle the impact of age and that of cancer diagnosis and treatment on functional status (FS) decline in older patients with cancer.

Materials and Methods: Patients with breast and colorectal cancer aged 50–69 years and aged ≥ 70 years who had undergone surgery, and older patients without cancer aged ≥ 70 years were included. FS was assessed at baseline and after 12 months follow-up, using the Katz index for activities of daily living (ADL) and the Lawton scale for instrumental activities of daily living (IADL). FS decline was defined as ≥ 1 point decrease on the ADL or IADL scale from baseline to 12 months follow-up.

Results: In total, 179 older patients with cancer (≥ 70 years), 341 younger patients with cancer (50–69 years) and 317 older patients without cancer (≥ 70 years) were included. FS decline was found in 43.6%, 24.6% and 28.1% of the groups, respectively. FS decline was significantly worse in older compared to younger patients with cancer receiving no chemotherapy (44.5% versus 17.6%, $p < 0.001$), but not for those who did receive chemotherapy (39.4% versus 30.8%, $p = 0.33$). Among the patients with cancer, FS decline was significantly associated with older age (OR 2.63), female sex (OR 3.72), colorectal cancer (OR 2.81), polypharmacy (OR 2.10) and, inversely, with baseline ADL dependency (OR 0.44).

Conclusion: Cancer treatment, and older age are important predictors of FS decline. The relation of baseline ADL dependency and chemotherapy with FS decline suggest that the fittest of the older patients with cancer were selected for chemotherapy.

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1. Introduction

Cancer mainly affects the older population [1]. In Europe, over 364,000 and 342,000 patients a year are diagnosed with breast and colorectal cancer, respectively [1]. At the time of diagnosis, 40% of patients

Abbreviations: FS, functional status; PFS, progression-free survival; OS, overall survival; ADL, Activities of daily living; IADL, Instrumental activities of daily living; KLIMOP, study (Cancer in Limburg Older Patients).

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with breast cancer and 60% of patients with colorectal cancer are aged ≥ 70 years [2]. With the aging of the population, the number of older patients with cancer is expected to rise further in the coming decades [2].

Evidence for the optimal treatment of patients with cancer is largely limited to younger patients or selected older patients with good overall health, while other older patients, especially those with poor performance status and comorbid conditions, have been underrepresented in clinical trials [3,4]. The International Society of Geriatric Oncology (SIOG) has reported that clinical trials often use endpoints inappropriate for older patients with cancer [5]. The most frequently investigated endpoints are still progression-free survival (PFS) and overall survival (OS) [3,4,6], while older patients often prefer preservation of independency as the most relevant endpoint [7,8]. Hence, additional endpoints besides PFS and OS, like maintaining an independent functional status (FS), should be investigated in older patients in order to choose the appropriate treatment for an older patient with cancer [7]. Previous

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studies have shown a positive association between functional independence, quality of life and survival, emphasizing the importance of studying FS in older patients with cancer [9,10]. FS declines with age and after cancer treatment. As a result, older patients with cancer are at higher risk of FS decline than older patients without cancer [11].

The aim of the present study was therefore to examine the impact of age and that of cancer diagnosis and treatment on FS decline in older patients with cancer.

2. Methods

2.1. Patients

Patients were selected from participants of the KLIMOP study (Cancer in Limburg Older Patients), a longitudinal cohort study that included older patients with cancer (aged ≥ 70 years), younger patients with cancer (aged 50–69 years), and participants without a previous diagnosis of cancer (aged ≥ 70 years) [12].

Participants were recruited between June 2010 and August 2014. Younger and older patients with cancer were recruited through nine academic and non-academic hospitals in Belgium and in the Netherlands. The participants without cancer were recruited through family practices from the same region as the patients with cancer. The general practitioners asked all eligible patients to participate until 20 patients per general practitioner agreed to participate.

The inclusion criteria were a new diagnosis of cancer (i.e. lung, prostate, gastrointestinal, or breast cancer), an estimated life expectancy of more than six months, and no previous diagnosis of cancer except for non-melanoma tumors of the skin. The exclusion criteria were inability to speak Dutch and a formal diagnosis of dementia.

In the present analysis, we included patients with breast and colorectal cancer who had undergone surgery, and all participants without a previous diagnosis of cancer. We excluded participants with other cancer types in order to pursue a more homogeneous study population. Patients who died, were lost to follow-up, or had missing functional status measurements at baseline or after 12 months of follow-up were excluded from the analysis.

The medical research ethics committees of KU Leuven, UZ Leuven (S52097-ML6279) and the Maastricht University Medical Center (NL414.068.10) approved the KLIMOP study. Written informed consent was obtained from all participants.

2.2. Demographic, Functional, and Clinical Characteristics

Demographic characteristics were collected within three months after cancer diagnosis and included age (years), gender, living situation (living together or alone), and educational level (age when leaving school). Functional characteristics included activities of daily living, using the Katz scale (ADL, cut-off for dependency ≥ 1) [13]; instrumental activity of daily living, using the Lawton scale (IADL, cut-off for dependency ≥ 1) [14]; cognitive function, using the mini mental state examination (MMSE, cut-off for cognitive impairment ≤ 23) [15]; depressive symptoms, using the geriatric depression scale-15 (GDS-15, cut-off for depressive symptoms ≥ 5) [16]; nutritional status, using body mass index (BMI, cut-offs for low BMI < 20 , normal BMI 20–30, and high BMI > 30) [17]; number of daily medications being used (cut-off for polypharmacy ≥ 5) [18,19]; comorbidity, using the diseases listed in the charlson comorbidity index (CCI) [20]; fatigue, using a visual analogue scale (VAS, cut-off for fatigue ≥ 4) [21,22]; and social support (available or not available). Clinical tumor characteristics were obtained from the medical charts and included cancer type (breast cancer, colorectal cancer), stage (stage I to II, stage III to IV) and cancer treatment (surgery, radiotherapy, hormone therapy, and chemotherapy).

2.3. Functional Status (FS) Decline

FS decline was defined as ≥ 1 point decrease on the Katz ADL scale [13] or the Lawton IADL scale [14] between baseline and 12 months follow-up. The Katz ADL scale contains six items (bathing, dressing, toileting, transferring, continence, and feeding). All items were scored as 0 (dependent) or 1 (independent). The Katz ADL score ranges from 0 (unable to perform any activity) to 6 (able to perform all activities) and ADL dependency was defined as being unable to perform one or more activities [13]. The Lawton IADL scale contains five items for men and eight items for women, namely using a telephone, shopping, preparing a meal, cleaning the house, preparing things in the house, doing the laundry, moving around outside the home, taking medications, and handling financial matters. All items were scored as 0 (dependent, able to perform activity with some help or not able to perform activity without help) or 1 (independent, able to perform activity). The Lawton IADL scale ranges from 0 (unable to perform any activity) to 5 and 8 for men and women, respectively (able to perform all activities). IADL dependency was defined as needing help or being unable to perform one or more activities [14].

2.4. Statistical Analysis

The primary endpoint of this analysis was the impact of age on FS decline in patients with cancer aged 50–69 years compared with patients with cancer aged ≥ 70 years. The secondary endpoint was the impact of cancer diagnosis and treatment on FS decline in patients with cancer and control patients without cancer aged ≥ 70 years. Demographic, clinical, and functional characteristics were described and compared using the chi-square test and Mann–Whitney, where appropriate.

Logistic regression analysis was performed with a non-step model in order to use the best model for FS decline (with $\alpha = 0.20$). Variables included in the analysis (coded as 0 or 1, unless otherwise specified) were age (50–69 years vs. ≥ 70 years), gender (male, female), cancer diagnosis (breast cancer, colorectal cancer), cancer stage (stage I or II, stage III or IV), chemotherapy (yes vs. no), baseline ADL (independent vs. dependent), baseline IADL (independent vs. dependent), polypharmacy (4 or less vs. higher scores), MMSE (24 or more vs. lower scores), GDS (4 or less vs. higher scores), body mass index (1 = 20–30; 2 = < 20 ; 3 = > 30), fatigue (3 or less vs. higher scores), living alone, and presence of caregiver. The collinearity of the models was analyzed with the variance inflation factor (VIF) in a regression model. In this model we did not detect collinearity for FS decline (VIF < 2.8). Comorbidity was not included in the model because it is clinically related to polypharmacy. The same predictors, except for cancer stage and treatment, were included in a logistic regression analysis for patients with cancer and control patients without cancer aged ≥ 70 years. The model calibration was assessed using the Hosmer and Lemeshow's goodness-of-fit test, and the discrimination of the model was based on the area under the receiver operating curve (AUC).

Sensitivity analyses to assess the influence of missing values for FS decline were performed, making a worst and best case scenario by merging all missing values as either a normal or an abnormal score.

Unadjusted and adjusted Odds Ratios (ORs) with 95% confidence intervals (CI) were calculated. We used SPSS (Statistical Package for the Social Sciences) version 21.0 for all analyses.

3. Results

Among the 1490 patients included in the KLIMOP study, 1217 had been diagnosed with breast or colorectal cancer or were older patients without cancer (Fig. 1). After 12 months, 22 of the patients (1.8%) had died, 63 (5.2%) had missing ADL and IADL data, and 295 (24.2%) were lost to follow-up.

Reasons for not participating at 12 months follow-up were personal problems (e.g. loss of a spouse), health problems (e.g. cancer

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