Functional status decline in older patients with breast and colorectal cancer after cancer treatment

van Abbema, Doris; van Vuuren, Arnée; van den Berkmortel, Franchette; van den Akker, Marjan; Deckx, Laura; Buntinx, Frank; van Kampen, Roel; Lambooij, Els; de Boer, Maaike; de Vos-Geelen, Judith; Tjan-Heijnen, Vivianne C

Published in:
Journal of geriatric oncology

DOI:
10.1016/j.jgo.2017.01.003

Creative Commons License (see https://creativecommons.org/use-remix/cc-licenses):
CC BY

Citation for published version (APA):
van Abbema, D., van Vuuren, A., van den Berkmortel, F., van den Akker, M., Deckx, L., Buntinx, F., ... Tjan-Heijnen, V. C. (2017). Functional status decline in older patients with breast and colorectal cancer after cancer treatment: a prospective cohort study. Journal of geriatric oncology, 8(3), 176-184. https://doi.org/10.1016/j.jgo.2017.01.003
Functional status decline in older patients with breast and colorectal cancer after cancer treatment: A prospective cohort study

Doris van Abbe ma,a,1, Arnée van Vuuren b, Franchette van den Berkmortel b, Marjan van den Akker c,d, Laura Deckx d,2, Frank Buntinx c,d, Roel van Kampen b, Els Lambooy e, Maaike de Boer a, Judith de Vos-Geelena, Vivianne C. Tjan-Heijenen a,

a Department of Medical Oncology, GROW - School for Oncology and Developmental Biology, Maastricht University Medical Center, Peter Debyelaan 25, 6229 HX, Maastricht, The Netherlands
b Department of Internal Medicine, Zuyderland Medical Center, Henri Dunantstraat 5, 6419 PC Heerlen-Geleen, The Netherlands
c Department of Family Medicine, Maastricht University, Peter Debyelaan 25, 6229 HX, Maastricht, The Netherlands
d Department of General Practice, KU Leuven, Kapucijnenvoer 33, PB 7001 3000 Leuven, Belgium
e Department of Internal Medicine, Máxima Medical Center, De Run 4060, 5504 DB, Veldhoven, The Netherlands

A R T I C L E   I N F O
A B S T R A C T

Article history:
Received 22 September 2016
Received in revised form 17 December 2016
Accepted 18 January 2017
Available online 31 January 2017

Keywords:
Colorectal cancer
Breast cancer
Chemotherapy
Older patients
Elderly
Activities of daily living
Instrumental activities of daily living
Functional status

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 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 independence 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
studies have shown a positive association between functional independency, 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 (SS2097-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 2 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, 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 a = 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 Odd 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...
recurrence), or other (e.g. too busy). Hence, the analysis included 837 patients: 179 older patients with cancer, 341 younger patients with cancer and 317 older patients without cancer. Compared to the older patients with cancer available for analysis, those with missing data or those lost to follow-up were more likely to be male (26.4% vs. 15.6%), more likely to have colorectal cancer (50.0% vs. 20.7%), and less likely to have stage I or II disease (59.1% vs. 73.2%). Younger patients with cancer with missing data or lost to follow-up were more likely to have colorectal cancer than those available for analysis (28.7% vs. 22.9%).

3.1. Baseline Characteristics

Baseline characteristics are described in Table 1. Compared to younger patients, older patients with cancer were less likely to be treated with chemotherapy (18.4% vs. 53.4%, \( p < 0.01 \)), more likely to be ADL- (50.3% vs. 28.4%, \( p < 0.001 \)) and IADL-dependent (33.6% vs. 23.6%, \( p < 0.03 \)), more likely to have polypharmacy (26.8% vs. 14.7%, \( p < 0.01 \)), more likely to have impaired cognition (10.1% vs. 2.6%, \( p < 0.01 \)), more likely to be living alone (33.6% vs. 14.7%, \( p < 0.001 \)), and more likely to have left school at a younger age (22.3% vs. 9.4%, \( p < 0.001 \)). On the other hand, younger patients with cancer were more likely to report depressive symptoms than older patients with cancer (12.3% vs. 6.1%, \( p < 0.03 \)) at baseline.

Compared to older patients without cancer, older patients with cancer were more likely to be female (84.4% vs. 61.5%, \( p < 0.001 \)), less likely to have polypharmacy (26.8% vs. 48.6%, \( p < 0.001 \)), more likely to be ADL-dependent (50.3% vs. 37.2%, \( p < 0.03 \)), and more likely to receive social support (65.4% versus 48.9%, \( p < 0.001 \)).

3.2. Impact of Age, Cancer Diagnosis, and Treatment

In the group of older patients with cancer, 78 patients (43.6%) declined in FS, against 84 (24.6%) in the group of younger patients with cancer, and 89 (28.1%) in the group of older patients without cancer. Thirty-three (18.4%) of the 179 older patients with cancer available for analysis received chemotherapy, compared to 182 (53.4%) of the 341 younger patients with cancer. FS decline was significantly worse for 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%, \( p = 0.33 \)) (Fig. 2).
Table 2 shows the results of the logistic regression analysis for FS decline for all patients with cancer, to assess the impact of aging. The characteristics associated with FS decline in the multivariate analysis were age > 70 years (odds ratio [OR] 2.63; 95% confidence interval [CI] 1.63–4.23), female sex (OR 3.72; 95% CI 1.59–8.71), colorectal cancer (OR 2.81; 95% CI 1.33–5.91), polypharmacy (OR 2.10; 95% CI 1.25–3.54), and, inversely, ADL dependency (OR 0.44; 95% CI 0.27–0.70); IADL decline was not predicted by colorectal cancer (OR...
1.58; 95% CI 0.68–3.66) or ADL dependency (OR 1.37; 95% CI 0.83–2.27). Similar predictors were found for ADL decline.

Table 3 presents the results of the logistic regression analysis for all older patients, assessing the impact of cancer. In the multivariate model, the risk of FS decline was higher in patients aged ≥80 years (OR 2.90; 95% CI 1.77–4.76), after cancer treatment (OR 1.77; 95% CI 1.19–2.63), polypharmacy (OR 2.36; 95% CI 1.47–3.82), and fatigue at baseline (OR 2.05; 95% CI 0.83–4.76).

**Fig. 2.** Percentage ADL decline, IADL decline, and functional status (FS) decline over a 12-months observation period.
4 Discussion

The aim of this study was to analyze the impact of age, cancer diagnosis, and treatment on FS decline in patients with cancer. In our study population, we found that FS decline was common among older patients with cancer. Almost half of the older patients with cancer reported FS decline, compared to a quarter of the younger patients with cancer. Important predictors of FS decline were cancer diagnosis and, within the patient group with cancer, higher age, female sex, colorectal cancer, and polypharmacy.

An unexpected finding in our study was that ADL dependency at baseline was a protective factor for FS decline in patients with cancer. This is in contrast with previous studies, where baseline functional dependency was a risk factor for FS decline [23]. It seems likely that part of this ADL dependency at baseline was caused by tumor-related complaints, which could have improved after specific antitumor treatment was provided or with supportive care measures such as radiotherapy for painful bone metastases or use of painkillers. Unfortunately, this data was not collected in our study. Another explanation might be a ceiling effect where ADL dependency at baseline was a protective factor for FS decline in patients with cancer. This is in contrast with previous studies, where baseline functional dependency at baseline was a protective factor for FS decline in patients with cancer.

We noted FS decline in 39.4% of the older patients with cancer who did not receive chemotherapy compared to 30.8% of patients younger patients with cancer, with FS decline in 17.6% of the patients who did receive chemotherapy. The opposite effect was seen in the younger patients with cancer who did not receive chemotherapy compared to 44.5% of the older patients with cancer. The opposite effect was seen in the younger patients with cancer who did not receive chemotherapy compared to 44.5% of the older patients with cancer. Important predictors of FS decline were cancer diagnosis and, within the patient group with cancer, higher age, female sex, colorectal cancer, and polypharmacy.

1.26–3.34). Similar predictors were found for ADL and IADL decline.

3.3 Sensitivity Analysis

Results changed slightly when adjusting the missing values as either a best or worst case scenario. Gender was not a significant factor when adjusting the missing values as best case scenario in all older patients, while cancer treatment was not a significant factor when adjusting the missing values as best case scenario in patients with cancer. Other results did not change (Additional Table S1, and S2).

Table 2 Logistic regression analysis for ADL decline, IADL decline, and functional status (FS) decline in older and younger cancer patients over a 12-month observation period.

| ADL decline | IADL decline | Functional status decline |
|-------------|--------------|--------------------------|
| OR (95% CI) | OR (95% CI)  | OR (95% CI)              |
| Age         |              |                          |
| 50-69 years | 1.00         | 1.00                     |
| ≥70 years   | 3.83 (1.86-7.89) | 2.16 (1.28-3.83)     |
| Gender      |              |                          |
| Male        | 1.00         | 1.00                     |
| Female      | 0.95 (0.53-1.69) | 3.35 (1.28-8.76)     |
| Cancer diagnosis |            |                          |
| Breast      | 1.00         | 1.00                     |
| Colorectal  | 1.89 (1.18-3.02) | 4.16 (1.77-9.79)     |
| Stage       |              |                          |
| I-II        | 1.00         | 1.00                     |
| III-IV      | 1.74 (1.06-2.83) | 1.29 (0.64-2.58)    |
| Chemotherapy |            |                          |
| No          | 1.00         | 1.00                     |
| Yes         | 1.19 (0.78-1.84) | 1.24 (0.67-2.31)    |
| Katz ADL (0–6) |            |                          |
| Independent | 1.00         | 1.00                     |
| Dependent   | 0.30 (0.18-0.52) | 0.16 (0.08-0.31)    |
| Lawton IADL (0–5/8) | | |
| Independent | 1.00         | 1.00                     |
| Dependent   | 1.69 (1.07-2.69) | 1.64 (0.93-2.88)   |
| Polypharmacy |            |                          |
| No (≤4)     | 1.00         | –                        |
| Yes (≥5)    | 1.79 (1.08-2.96) | 2.07 (1.12-3.85)    |
| Cognition (MMSE, 0–30) | | |
| Normal (≥24) | 1.00         | 1.00                     |
| Impaired (≤23) | 0.87 (0.32-2.37) | 1.02 (0.40-2.62)   |
| Depressive symptoms (GDS) | | |
| None (≤4)   | 1.00         | 1.00                     |
| Mild or severe (≥5) | 0.59 (0.26-1.36) | 0.73 (0.33-1.60)   |
| Body mass index (BMI) | | |
| Normal (20–30) | 1.00         | 1.00                     |
| Low (<20)   | 0.67 (0.23-1.97) | 0.52 (0.11-2.42)    |
| High (>30)  | 1.83 (1.10-3.04) | 2.23 (1.25-3.97)   |
| Fatigue (0–10) |            |                          |
| No (≤3)     | 1.00         | 1.00                     |
| Yes (≥4)    | 1.21 (0.75-1.84) | 1.36 (0.81-2.28)    |
| Living situation | | |
| Alone       | 1.00         | 1.00                     |
| Living together, institutionalized | 1.00 | 1.00 |
| Social support |            |                          |
| Not available | 1.00         | 1.00                     |
| Available   | 0.93 (0.52-1.67) | 0.97 (0.53-1.78)    |
| Hosmer en Lemeshow test | | |
| Area under the curve | | |
| 14.25 (p = 0.08) | 12.97 (p = 0.11) | 10.26 (p = 0.17)   |
| 0.76 (0.71-0.81) | 0.69 (0.62-0.75) | 0.68 (0.63-0.73)   |

OR1, univariate analysis; OR2, multivariate analysis.

Significant OR’s are indicated in bold.

ADL, activities of daily living; IADL, instrumental activities of daily living; MMSE, Mini Mental State Examination; GDS-15, Geriatric Depression Scale-15.
correctly selected for chemotherapy, and more intensive chemotherapy may have been given to the younger patients with cancer.

Ronning et al. [24] investigated the impact of surgery in 84 older patients with colorectal cancer, and found that ADL and IADL decline were present in 31% and 69% of the patients, respectively. However, conflicting results have been reported regarding the impact of chemotherapy on FS decline, with studies reporting either a negative effect or no effect [30].

In our study, we also analyzed the impact of cancer diagnosis among older patients with cancer compared to control patients without cancer in the same age group, and found that cancer treatment was an important predictor of FS decline in a large prospective cohort of patients with cancer and healthy controls. They concluded that FS decline was more profound in patients with cancer than in healthy controls. In their recent year after cancer diagnosis, and continued to decline after one year. Besides cancer and age, important predictors of FS decline found by Petrick et al. were educational level, comorbidity, obesity, smoking, and lack of health insurance. Previous studies of FS decline in older patients with cancer found that comorbidity [11], depressive symptoms [25], IADL dependency [25], and obesity [11] were associated with FS decline. This could not be confirmed in the present study. It should be noted that lack of health insurance is non-existent in the Netherlands and was therefore not included in our analyses. Consistent

Table 3

|                | ADL decline | IADL decline | Functional status decline |
|----------------|-------------|--------------|--------------------------|
|                | OR1 (95% CI) | OR2 (95% CI) | OR1 (95% CI) | OR2 (95% CI) | OR1 (95% CI) | OR2 (95% CI) |
| Age            |             |              |              |              |              |              |
| 70–79 years    | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| ≥80 years      | 2.08 (1.33–3.26) | 2.96 (1.67–5.25) | 2.96 (1.91–4.59) | 2.87 (1.63–5.05) | 2.57 (1.75–3.78) | 2.90 (1.77–4.76) |
| Gender         |             |              |              |              |              |              |
| Male           | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Female         | 2.29 (1.32–3.98) | 0.81 (0.45–1.45) | 1.35 (0.84–2.18) | 0.92 (0.52–1.62) | 1.93 (1.25–2.98) | 1.58 (0.95–2.64) |
| Cancer treatment |           |              |              |              |              |              |
| No             | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Yes            | 1.85 (1.19–2.89) | 2.59 (1.43–4.71) | 2.13 (1.38–3.28) | 2.42 (1.37–4.29) | 1.98 (1.35–2.90) | 1.77 (1.19–2.63) |
| Katz ADL (0–6) |             |              |              |              |              |              |
| Independent    | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Dependent      | 0.62 (0.39–0.99) | 1.52 (0.86–2.66) | 2.32 (1.51–3.57) | 1.55 (0.89–2.68) | 1.16 (0.80–1.69) | 0.67 (0.40–1.12) |
| Lawton IADL (0–5/8) |       |              |              |              |              |              |
| Independent    | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Dependent      | 1.91 (1.22–2.99) | 0.60 (0.33–1.12) | 1.13 (0.72–1.75) | 0.61 (0.34–1.11) | 1.25 (0.85–1.85) | 0.82 (0.49–1.39) |
| Polypharmacy   |             |              |              |              |              |              |
| No (≤4)        | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Yes (≥5)       | 1.78 (1.15–2.78) | 2.46 (1.42–4.25) | 2.18 (1.42–3.35) | 2.46 (1.42–4.25) | 1.95 (1.35–2.85) | 2.36 (1.47–3.82) |
| Cognition (MMSE, 0–30) |       |              |              |              |              |              |
| Normal (≥24)   | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Impaired (≤23) | 1.65 (0.79–3.43) | 0.86 (0.35–2.12) | 1.58 (0.77–3.25) | 1.85 (0.97–3.52) | 1.24 (0.57–2.72) | 1.00         |
| Depressive symptoms (GDS) |       |              |              |              |              |              |
| None (≤4)      | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Mild or severe (≥5) | 1.11 (0.51–2.41) | 1.80 (0.91–3.58) | 1.22 (0.64–2.34) | 1.00         | 1.00         | 1.00         |
| Body mass index (BMI) |       |              |              |              |              |              |
| Normal (20–30) | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Low (<20)      | 0.56 (0.33–0.98) | 0.80 (0.48–1.40) | 0.63 (0.39–1.01) | 1.41 (0.49–4.02) | 1.00         | 1.00         |
| High (>30)     | 0.47 (0.13–1.75) | 1.76 (0.60–5.13) | 0.89 (0.35–2.29) | 1.65 (0.93–2.93) | 1.00         | 1.00         |
| Fatigue (0–10) |             |              |              |              |              |              |
| No (≤3)        | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Yes (≥4)       | 2.30 (1.37–3.86) | 2.42 (1.35–4.32) | 2.52 (1.50–4.22) | 2.29 (1.31–4.02) | 2.21 (1.45–3.39) | 2.05 (1.26–3.34) |
| Living situation |           |              |              |              |              |              |
| Alone          | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Living together, institutionalized | 0.99 (0.62–1.59) | 1.39 (0.87–2.24) | 0.94 (0.64–1.40) | 1.00         | 1.00         | 1.00         |
| Social support |             |              |              |              |              |              |
| Not available  | 1.00        | 1.00         | 1.00         | 1.00         | 1.00         | 1.00         |
| Available      | 1.19 (0.74–1.91) | 1.27 (0.79–2.04) | 1.30 (0.87–1.96) | 1.00         | 1.00         | 1.00         |
| Hosmer-Lemeshow test | 6.95 (p = 0.54) | 5.74 (p = 0.68) | 13.20 (p = 0.10) | 1.00         | 1.00         | 1.00         |
| Area under the curve | 0.74 (0.69–0.80) | 0.74 (0.69–0.80) | 0.72 (0.67–0.78) | 1.00         | 1.00         | 1.00         |

OR1, univariate analysis; OR2, multivariate analysis.
Significant ORs are indicated in bold.
ADL, activities of daily living; IADL, instrumental activities of daily living; MMSE, Mini Mental State Examination; GDS-15, Geriatric Depression Scale-15.
with previous studies [11,23,24], we found that age was an important predictor of FS decline in patients with cancer. The main strengths of our study include its longitudinal design, respectable sample size, and the analysis of three different patient groups, enabling us to compare FS decline in older patients with cancer with that in younger patients with cancer and that in older patients with cancer with that in older patients without cancer. This study also has several limitations. After 12 months of follow-up, data were incomplete for 31% of patients, although this is comparable with other longitudinal cohort studies that included older patients with cancer [31]. The older and younger patients with cancer not available for analysis were more likely to have colorectal cancer than those available for analysis. This may have caused an underestimation of FS decline in our study population, because patients with colorectal cancer who were evaluable showed a higher risk of FS decline compared to patients with breast cancer [11]. Another limitation was the timing of our baseline interview. For practical reasons we included patients within a time frame of 0 to 3 months after diagnosis. In fact, some of the patients had already started treatment at the time of the baseline interview, and this could have affected their baseline health and FS. Another limitation is the lack of multiple time points to evaluate functional status, and the exclusion of non-surgical patients. In conclusion, FS decline is common among older patients with cancer. Important overall predictors of FS decline are age and cancer diagnosis. The high percentage of FS decline in older patients with cancer underlines the need for more studies to investigate the impact of cancer treatment on FS decline in this specific group. Maintaining FS could play an important role in improving survival and quality of life and in developing a personalized treatment plan for the older patients with cancer.

Disclosures and Conflict of Interest Statements

The authors have no conflicts to report.

Author Contributions

Study Concept: F van den Berkmortel, M van den Akker, L Deckx, F Buntinx, VC Tjan-Heijnen.
Study Design: F van den Berkmortel, M van den Akker, L Deckx, F Buntinx, VC Tjan-Heijnen.
Data Acquisition: D van Abbema, A van Vuuren, M van den Akker, L Deckx.
Quality Control of Data and Algorithms: D van Abbema, A van Vuuren, M van den Akker, L Deckx.
Data Analysis and Interpretation: D van Abbema, A van Vuuren, F van den Berkmortel, M van den Akker.
Statistical Analysis: D van Abbema, A van Vuuren, M van den Akker.
Manuscript Preparation: D van Abbema, A van Vuuren, F van den Berkmortel, M van den Akker, VC Tjan-Heijnen.
Manuscript Editing: D van Abbema, A van Vuuren, F van den Berkmortel, M van den Akker, L Deckx, F Buntinx, R van Kampen, E Lamboori, M de Boer, J de Vos-Geelen, VC Tjan-Heijnen.
Manuscript Review: D van Abbema, A van Vuuren, F van den Berkmortel, M van den Akker, L Deckx, F Buntinx, R van Kampen, E Lamboori, M de Boer, J de Vos-Geelen, VC Tjan-Heijnen.

Acknowledgements

The KLIMOP study was supported by the European Union / Interreg IV Gronsgeno Vlaanderen - Nederland (IVA-VLANED-3.46) and the Vlaams League tegen Kanker (Flemish League against Cancer) (10482). The authors had complete authority over design, execution, analysis, and interpretation of the study.

We wish to thank all the participants of the KLIMOP study for their contributions. Finally, we wish to thank the research group of the KLIMOP study, the nurses and physicians for their support and advice.

Appendix A. Supplementary Data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jgo.2017.01.003.

References

[1] Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JW, Comber H, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013;49(6):1374–403.
[2] de Moor JS, Mariotti AB, Parry C, Alfaro CM, Padgett L, Kent EE, et al. Cancer survivors in the United States: prevalence across the survivorship trajectory and implications for care. Cancer Epidemiol Biomarkers Prev 2013;22(4):561–70.
[3] Aapro MS, Kohn HE, Cohen HJ, Externermann M. Never too old? Age should not be a barrier to enrollment in cancer clinical trials. Oncology 2005;10(3):198–204.
[4] Hurria A, Unger JM, Crowley J, Colman Jr CA, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med 1999;341(27):2061–7.
[5] Wildiers H, Mauer M, Pallis A, Hurria A, Mobale SG, Luciani A, et al. End points and trial design in geriatric oncology research: a joint European organisation for research and treatment of cancer-alliance for clinical trials in oncology-international society of geriatric oncology position article. J Clin Oncol Off J Am Soc Clin Oncol 2013;31(29):3711–8.
[6] van Bekkum ML, van Munster BC, Thunnissen PL, Smorenburg CH, Hamaker ME. Current palliative chemotherapy trials in the elderly neglect patient-centred outcome measures. J Geriatr Oncol 2015;6(1):15–22.
[7] Weddington U, Peinetta L, Hoffken K. Quality-of-life in elderly patients with cancer: a short review. Eur J Cancer 2007;43(15):2203–10.
[8] Jorgensen ML, Young JM, Solomon MJ. Adjuvant chemotherapy for colorectal cancer: age differences in factors influencing patients’ treatment decisions. Patient Prefer Adherence 2013;7:827–34.
[9] Hurria A, Zuckerman E, Panagopoulos KS, Forster M, D’Andrea G, Dang C, et al. A prospective, longitudinal study of the functional status and quality of life of older patients with breast cancer receiving adjuvant chemotherapy. J Am Geriatr Soc 2006;54(7):1119–24.
[10] Puts MTE, Monette J, Giro E, Wolfsön C, Monette M, Battist G, et al. Quality of life during the course of cancer treatment in older newly diagnosed patients. Results of a prospective pilot study. Ann Oncol 2011;22(4):916–23.
[11] Petrick JL, Reeve BB, Kucharska-Newton AM, Foraker RE, Plauz EA, Stearns SC, et al. Functional status declines among cancer survivors: trajectory and contributing factors. J Geriatr Oncol 2014;5(4):359–67.
[12] Bockx L, van Abbema D, Nelsensen K, Danilis L, Stienen P, Bultens P, et al. Study protocol of KLIMOP: a cohort study on the wellbeing of older cancer patients in Belgium and the Netherlands. BMC Public Health 2011;11(1):823.
[13] Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc 1983;31(12):721–7.
[14] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9(3):179–86.
[15] Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12(3):189–98.
[16] Yasavage JG, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17(1):37–40.
[17] Committee ReaWE. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee; 1995. p. 5012–3054 (Print; 5012–3054).
[18] Turner JP, Jamsen KM, Shakib S, Singhal N, Prowse R, Bell JS. Polypharmacy cut-off and outcomes: a systematic review. Curr Med Res Opin 2009;25(12):2031–40.
[19] Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. The Value of Fatigue Severity to Rule Out Depression in Older Adult Patients With Cancer. Oncol Nurs Forum 2015;42(4):E302–9.
[20] Cornette P, Swine C, Mallinson B, Giller J, Meert P, D’Hoore W. Early evaluation of the risk of functional decline following hospitalization of older patients: development of a predictive tool. Eur J Public Health 2006;16(2):203–8.
[21] Bannon R, Wylle TR, Jordhsey MS, Neshbonak A, Bakka A, Sefjellof I, et al. Frailty indicators and functional status in older patients after colorectal cancer surgery. J Geriatr Oncol 2014;5(1):26–32.
[22] Hoppe S, Rainfaray M, Fonck M, Hoppenreys L, Blanc J-F, Ceccaldi J, et al. Functional Decline in Older Patients With Cancer Receiving First-Line Chemotherapy. J Clin Oncol Off J Am Soc Clin Oncol 2013.
[23] Brain EC, Mertens C, Giro E, Rousseau F, Bler E, Abadie S, et al. Impact of liposomal doxorubicin-based adjuvant chemotherapy on autonomy in women over 70 with
hormone-receptor-negative breast carcinoma: A French Geriatric Oncology Group (GERICO) phase II multicentre trial. Crit Rev Oncol Hematol 2011;80(1):160–70.

Alibhai SM, Breunis H, Timilshina N, Brignardello-Petersen R, Tomlinson G, Mohamedali H, et al. Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age. J Geriatr Oncol 2015;6(4):262–71.

Manokumar T, Atiz S, Breunis H, Rizvi SF, Joshua AM, Tannock IF, et al. A prospective study examining elder-relevant outcomes in older adults with prostate cancer undergoing treatment with chemotherapy or abiraterone. J Geriatr Oncol 2016;7(2):81–9.

Buurman BM, van Munster BC, Korevaar JC, de Haan RJ, de Rooij SE. Variability in measuring (instrumental) activities of daily living functioning and functional decline in hospitalized older medical patients: a systematic review. J Clin Epidemiol 2011;64(6):619–27.

Hoeben KW, van Steenbergen LN, van de Wouw AJ, Rutten HJ, van Sproosen DJ, Janssen-Heijnen ML. Treatment and complications in elderly stage III colon cancer patients in the Netherlands. Ann Oncol 2013;24(4):974–9.

Banks J, Muriel A, Smith JP. Attrition and health in ageing studies: Evidence from ELSA and HRS. Longit Life Course Stud 2011;2(2).