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Functional decline in older patients with cancer receiving chemotherapy: A multicenter prospective study

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ABSTRACT

Objectives: This study aims to evaluate the evolution of functional status (FS) 2 to 3 months after initiation of chemotherapy, to identify factors associated with functional decline during chemotherapy treatment and to investigate the prognostic value of functional decline for overall survival (OS).
Patients and Methods: Patients ≥70 years with a malignant tumor were included when chemotherapy was initiated. All patients underwent a geriatric assessment (GA) including FS measured by Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). FS of patients was followed by repeating ADL and IADL to identify functional decline.
Results: From 10/2009 until 07/2011, 439 patients were included. At follow-up, ADL and IADL data were available for 387 patients. Functional decline in ADL and IADL was observed in 19.9% and 41.3% of the patients respectively. In multivariable logistic regression analysis, baseline factors associated with decline in ADL are abnormal nutritional status (OR:2.02) and IADL dependency (OR:1.76). Oncological setting (disease progression/relapse vs new diagnosis) (OR:0.59) is the only determinant of decline in IADL. Functional decline in ADL is strongly prognostic for OS (logrank p-value < .0001; Wilcoxon p-value < .0001) with HR 2.34 and functional decline in IADL is also prognostic for OS but less prominent with HR 1.25.
Conclusions: Functional decline occurs in about a third of older patients with cancer receiving chemotherapy and is associated with GA components. It strongly predicts survival, the most prominent for ADL. This knowledge can be used to identify older persons with cancer receiving chemotherapy eligible for interventions to prevent functional decline.

1. Introduction

Maintenance of functional status (FS) is a key issue for older persons, certainly for those diagnosed with cancer [1]. Functional impairment has been independently associated with increased comorbidities [2] and shorter survival [3] and can lead to higher dependency, institutionalisation, and decreased quality of life [3,4]. 'Oncological' tools like the Karnofsky [5] or Eastern Cooperative Oncology group Performance Status (ECOG-PS) [6] scales reflect FS in a very simplistic way, and were not specifically developed and validated in the older population [1,7]. More sophisticated and age-adapted tools used in geriatric medicine are Katz's Activities of Daily Living (ADL) scale [8] and Lawton's Instrumental Activities of Daily Living (IADL) scale [9].

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The assessment of FS is an integral part of the comprehensive geriatric assessment (CGA) which is the cornerstone of current geriatric medicine [10], and also recommended by the International Society of Geriatric Oncology (SIOG) and the European Organisation for Research and Treatment of Cancer (EORTC) in the care for older patients with cancer [7,11]. CGA is defined as a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long-term follow-up [12].

Repeated assessment of FS over time gives treating physicians the opportunity to identify functional decline, which is a major threat for older persons in general [13] with increased risk for hospital and nursing home admission and mortality [14–16]. Functional decline is becoming an important health care focus for older patients in general during cancer treatment and more specific for older patients receiving chemotherapy [17,18]. In older patients receiving chemotherapy, the treatment is considered as a strong stressor that will reveal which patients have sufficient functional reserve to maintain functioning [19,20].

While the number of older patients with cancer is expected to increase [21,22], little is known about the evolution of FS during chemotherapy treatment. A better understanding of this evolution may allow the possibility to predict functional decline which is crucial because it could allow preventive measures for patients at risk [1,10,23].

Therefore, the aim of this study is to evaluate the evolution of FS in older patients with cancer 2 to 3 months after initiation of chemotherapy, to identify factors associated with functional decline during chemotherapy treatment and to investigate the prognostic value of functional impairments/decline for overall survival (OS).

2. Patients and Methods

2.1. Patient Population

The patient population in the current study has been described in detail elsewhere [24]. In summary, this was a prospective, non-interventional cohort study, performed in two academic hospitals in Belgium from October 2009 till July 2011. Patients 70 years and older with a malignant tumor, were approached for inclusion during a hospital visit by a trained nurse at diagnosis or at disease progression/relapse, when a cancer treatment decision had to be made. Disease progression/relapse was defined as progression under treatment or relapse after a treatment free interval. Inclusion was limited to six tumor types: breast, colorectal, ovarian, lung, prostate cancer and hematologic malignancies. The study was approved by the Ethical Committee of both participating hospitals (University Hospitals Leuven and University Hospital Brussel; B32220096771) and written informed consent was obtained from all patients or their caregiver prior to enrolment in the study. For the present study, we performed a subanalysis on the patients receiving chemotherapy.

2.2. Geriatric Screening and Assessment

A geriatric screening and assessment was performed in all patients by a trained nurse at baseline [24]. In brief, geriatric screening was performed by the Flemish version of the Triage Risk Screening Tool (fTRST) (≥1 is abnormal) [24–26] and G8 (≤14 is abnormal) [24,27,28]. The geriatric assessment (GA) comprised demographic and social data, such as age (categorized in 70–74/75–79/≥80), gender and living situation (living alone versus living with help).

Functional status (FS) was evaluated using Katz's Activities of Daily Living (ADL) scale [8] and Lawton's Instrumental Activities of Daily Living (IADL) scale [9]. The Katz scale includes six items (bathing, dressing, toileting, transferring, continence and feeding), with a score for each item ranging from one (able to perform the activity) to four (unable to perform the activity). Total score ranged from 6 (fully independent; no impairments) to 24 (fully dependent; 6 impairments) with dependency in ADL defined as a score of >6. The Lawton scale includes eight items (ability to use the telephone, shopping, cooking, housekeeping, doing laundry, responsibility of own medication, mode of transportation and ability to handle finances), with a score for each item of zero (low function, dependent, impairment) or one (high function, independent, no impairment). Because some of these items (cooking, housekeeping and doing laundry) are mostly done by women, these three items were not assessed in males in the original form, so the total score ranged from zero to five for men and from zero to eight for women. Consequently, dependency in IADL is defined as a score of <5 (male) or <8 (female).

Fall history was evaluated by asking the number of falls and fall-related injuries in the past 12 months (presence of falls vs absence) [29,30]. Cognition was evaluated using the Mini Mental State Examination (MMSE) (<24 is abnormal) [31] and risk for depression by the 15-item Geriatric Depression Scale (GDS-15) (≥5 is abnormal) [32]. Nutritional status was assessed using the Mini Nutritional Assessment-Short Form (MNA-SF) (≤11 is abnormal) [33,34]. The Charlson Comorbidity Index (CCI) (≥1 is abnormal) [35] was used to describe the comorbidities. Self-perceived fatigue was assessed using the Mobility-Tiredness Test (Mob-T) (presence of fatigue is abnormal) [36] and pain was evaluated with the Visual Analogue Scale (VAS) (≥1 is abnormal) [37]. Classical oncological parameters such as Eastern Cooperative Oncology Group - Performance Status (ECOG-PS) (categorized in 0–1 vs 2–4) [6], tumor characteristics (type and stage) and treatment details (presence of surgery/radiotherapy) were recorded. The number of drugs (www.bcfi.be) taken during the week before inclusion was recorded to detect polypharmacy (≥5 different drugs).

2.3. Functional Decline and Survival

FS of patients was followed by repeating ADL and IADL two to three months after initiation of chemotherapy. A questionnaire was sent to the patient, asking to report the current situation in these domains. When the questionnaire didn't return, patients were contacted by telephone or contacted in the hospital in person to complete the follow-up data. Functional decline in ADL was defined as an increase of two or more points on the total score and in IADL as a decrease of one or more points on the total score [23,24,38,39]. Secondly, the evolution of FS was evaluated for all individual ADL and IADL items. An increase of one or more points on an individual ADL item or a decrease in one or more points in an individual IADL item was considered as functional decline. Survival data were collected for all patients included in February 2016.

2.4. Statistical Analysis

All analyses were performed with SAS v9.3. All statistical tests were two-sided. For continuous data, mean, standard deviation, median, 95% confidence intervals and range were assessed. For categorical data, frequency was assessed as well as the 95% confidence interval.

Identification of factors associated with functional decline was performed for ADL and IADL separately by univariate logistic regressions. The following baseline categorical variables were used as defined above: age, living situation, fTRST, G8, oncological setting, FS by ADL and IADL, fall history, MMSE, GDS, MNA-SF, CCI, MOB-T, pain, ECOG-PS, polypharmacy, presence of surgery/radiotherapy.

Multivariable logistic regressions were conducted on functional decline in ADL and IADL separately, 2 to 3 months after initiation of chemotherapy, using stepwise variable selection and p-value to enter and stay in the model of 0.05. Only the variables which were significant in the univariate setting were considered for the multivariable regressions. Odds ratio's with 95% confidence limits for the significant variables are reported. Multiple collinearity was investigated for the independent variables used in the regressions, with variance inflation factor (VIF's) calculations, and was not detected so not further discussed.