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

Cindy Kenis^{a,d}, Lore Decoster^b, Julie Bastin^a, Hannelore Bode^a, Katrien Van Puyvelde^c, Jacques De Grève^b, Godelieve Conings^b, Katleen Fagard^d, Johan Flamaing^{d,e}, Koen Milisen^{d,f}, Jean-Pierre Lobelle^g, Hans Wildiers^{a,h,*}

^a Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium

^b Department of Medical Oncology, Oncologisch Centrum, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium

^c Frailty in Ageing (FRIA) Research Group & Gerontology Department, Vrije Universiteit Brussel, Brussels, Belgium

^d Department of Geriatric Medicine, University Hospitals Leuven, Leuven, Belgium

^e Department of Clinical and Experimental Medicine, KU Leuven, Belgium

^f Department of Public Health and Primary Care, Academic Centre for Nursing and Midwifery, KU Leuven, Belgium

^g Consultant in Statistics, Beemem, Belgium

^h Department of Oncology, KU Leuven, Belgium

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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.

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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].

* Corresponding author at: Department of General Medical Oncology, University Hospitals Leuven, Herestraat 49, 3000, Leuven, Belgium. Tel.: +32 16 34 69 20; fax: +32 16 34 69 01.

E-mail addresses: cindy.kenis@uzleuven.be (C. Kenis), lore.decoester@uzbrussel.be (L. Decoster), julie_bastin@hotmail.com (J. Bastin), hannelore.bode@gmail.com (H. Bode), katrien.vanpuyvelde@asz.be (K. Van Puyvelde), jacques.degreve@uzbrussel.be (J. De Grève), godelieve.conings@uzbrussel.be (G. Conings), katleen.fagard@uzleuven.be (K. Fagard), johan.flamaing@uzleuven.be (J. Flamaing), koen.milisen@kuleuven.be (K. Milisen), jeanpierre.lobelle@gmail.com (J.-P. Lobelle), hans.wildiers@uzleuven.be (H. Wildiers).

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.bcf.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.

OS, defined as the time from study entry until death (any cause) is described by Kaplan Meier plots and comparisons are made by logrank and Wilcoxon's test. Data were censored at the date of last contact. A Cox proportional hazard regression with functional decline in ADL and IADL separately as the independent variables, was conducted for the OS analysis with mature data. Proportional hazard assumption was verified by inspection of the Kaplan Meier plots and of the log[–log (survival probability)] versus log(time) plots, and the curves in both plots were parallel. No further correction was needed. Secondly, a multivariable Cox regression analysis was performed with the following variables: age, tumor type, functional decline in ADL, functional decline in IADL, FS by ADL and IADL, living situation, fall history, fatigue by MOB-T, MMSE, GDS, MNA-SF, CCI and polypharmacy. Hazard ratio's with 95% confidence limits were calculated in both regressions.

3. Results

3.1. Patient and clinical characteristics

For participation in the study, 1056 patients were approached. Of these patients, 54 patients refused to participate and 65 patients did not meet the inclusion criteria (mostly not being progressive, no invasive tumor diagnosed or primary origin of the tumor different from the six selected tumor types). Written informed consent was given by 931 patients and six caregivers, resulting in 937 patients included, of which 439 received chemotherapy (Fig. 1). The median age was 75 years (range: 70–95), and 57.6% were female. Hematologic malignancies were the most common diagnoses, accounting for 26.4% of the patients, followed by colorectal cancer (24.6%) and breast cancer (23.7%). Within the hematologic malignancies, non-Hodgkin lymphoma was the most common subtype (29.4%). At the moment of inclusion in the study, 55.6% had a newly diagnosed cancer, whereas 44.4% had disease progression/relapse. Comorbidities were present in 231 patients: 26.4% ($n = 116$) had score 1 and 26.2% ($n = 115$) had score ≥ 2 on the CCI. The most common comorbidities were congestive heart failure ($n = 73$; 31.6%), diabetes mellitus without complications ($n = 55$; 23.8%), secondary malignancy ($n = 51$; 22.1%), myocardial infarction ($n = 38$; 16.5%) and chronic pulmonary disease ($n = 35$; 15.2%). Further

patient and clinical characteristics are listed in Table 1. At baseline 205 (46.7%) patients reported dependency in ADL and 244 (55.6%) patients in IADL. Further results of the geriatric screening and assessment are shown in Table 2.

3.2. Evolution of functional status after initiation of chemotherapy

Two to 3 months after initiation of chemotherapy, data of 387 patients receiving chemotherapy were available for ADL and IADL (88.1%). In these patients functional decline in ADL was observed in 19.9% of the patients and in IADL in 41.3% of the patients. The evolution of FS related to the baseline FS is described in Fig. 2. There was no significant difference between the baseline independent and the baseline dependent group for functional decline in ADL ($p = 0.126$) and IADL ($p = 0.389$).

Considering the individual ADL components, patients declined most on the activities bathing (17.3%), dressing (17.3%) and continence (15.8%). Considering the individual IADL components, female older patients declined most on the activities cooking (28.1%), mode of transportation (25.0%) and shopping (23.7%), and male older patients declined most on mode of transportation (21.4%), shopping (20.1%) and responsibility of own medication (17.6%) (Table 3).

A more in depth analysis on functional decline related to tumor type (all patients) and staging of the tumor (for carcinoma patients only), integrating three categories of FS (improvement, stable, decline) shows that the highest rates of functional decline in ADL and IADL are present in patients with lung cancer (26.3%; 52.6% respectively) and ovarian cancer (30.2%; 44.2% respectively), followed by patients with hematologic malignancies and breast cancer. The results of this analysis are displayed in detail in the appendix of this article (see Appendices A and B).

3.3. Factors associated with functional decline in ADL and IADL

Table 4 describes univariate and multivariable analysis of factors associated with functional decline in ADL and IADL in the group of patients receiving chemotherapy ($n = 387$). Independent factors associated with functional decline in ADL were abnormal nutritional status measured by MNA-SF (OR:2.02; 95%CI:1.10–3.71), and baseline dependency in IADL activities (OR:1.76; 95%CI:1.03–2.99). Oncological setting (disease

Fig. 1. Flow-chart of patient selection.

Table 1
Patient and clinical characteristics.

Age, years (median(range))			Patients receiving chemotherapy			
			n = 439	75 (70–95)		
				n	%	95%CI
Gender	- Female		n = 439	253	57.6	53.0–62.3
	- Male			186	42.4	37.7–47.0
Tumor type	- Carcinoma	- Breast	n = 439	104	23.7	19.7–27.7
		- Colorectal		108	24.6	20.6–28.6
		- Lung		44	10.0	7.2–12.8
		- Ovarian		48	10.9	8.0–13.9
		- Prostate		19	4.3	2.4–6.2
	- Hematologic malignancies			116	26.4	22.3–30.5
Oncological setting	- New diagnosis		n = 439	244	55.6	50.9–60.2
	- At disease progression/relapse			195	44.4	39.8–49.1
Carcinoma	- Stage	- I	n = 323	5	1.5	0.2–2.9
		- II		34	10.5	7.2–13.9
		- III		62	19.2	14.9–23.5
		- IV		222	68.7	63.7–73.8
	- Treatment received ^a	- Surgery		107	33.1	28.0–38.3
		- Chemotherapy		323	100.0	100–100
		- Radiotherapy		60	18.6	14.3–22.8
		- Hormonal therapy		29	9.0	5.9–12.1
Hematologic malignancies	- Setting	- Curative	n = 116	45	38.8	29.9–47.7
		- Palliative		71	61.2	52.3–70.1
	- Treatment received ^a	- Surgery		0	0.0	0–0
		- Chemotherapy		116	100.0	100–100
		- Radiotherapy		3	2.6	0–5.5
Comorbidity	CCI (0–37)	- No comorbidities (score 0)	n = 439	208	47.4	42.7–52.1
		- Comorbidity score 1		116	26.4	22.3–30.5
		- Comorbidity score ≥ 2		115	26.2	22.1–30.3
Performance status	ECOG-PS (0–5)	- Score 0–1	n = 439	330	75.2	71.1–79.2
		- Score 2–4		109	24.8	20.8–28.9
Pain	VAS (0–10)	- No pain: score = 0	n = 438	205	46.8	42.1–51.5
		- Mild pain: score = 1–3		69	15.8	12.3–19.2
		- Pain to treat: score ≥ 4		164	37.4	32.9–42.0
Polypharmacy		- 0–4 different drugs	n = 427	220	51.5	46.8–56.3
		- ≥ 5 different drugs		207	48.5	43.7–53.2

Legend: CI = confidence interval; CCI = Charlson Comorbidity Index; ECOG PS = Eastern Cooperative Oncology Group Performance Status; VAS = Visual Analogue Scale.

^a Treatment received = patients may have received a combination of treatment modalities.**Table 2**
Results of the baseline geriatric screening and assessment.

			Patients receiving chemotherapy			
Screening	Cut-off	Score		n	%	95%CI
fTRST (0–6)	≥ 1	- Absence of a geriatric risk profile: score 0	n = 439	85	19.4	15.7–23.1
		- Presence of a geriatric risk profile: score ≥ 1		354	80.6	76.9–84.3
G8 (0–17)	≤ 14	- Absence of a geriatric risk profile: score > 14	n = 439	110	25.1	21.0–29.1
		- Presence of a geriatric risk profile: score ≤ 14		329	74.9	70.9–79.0
GA	Item/instrument	Score		n	%	95%CI
Social data	Living situation	- Living alone	n = 439	117	26.7	22.5–30.8
		- Living with help		322	73.3	69.2–77.5
Functional status	ADL (6–24)	- Independent: score 6	n = 439	234	53.3	48.6–58.0
		- Dependent: score ≥ 7		205	46.7	42.0–51.4
	IADL (0–5/8)	- Independent: score 8 (female) or 5 (male)	n = 439	195	44.4	39.8–49.1
		- Dependent: score < 8 (female) or 5 (male)		244	55.6	50.9–60.2
	Fall history in the past 12 months	- No falls	n = 439	321	73.1	69.0–77.3
		- ≥ 1 fall		118	26.9	22.7–31.0
Fatigue	MOB-T (0–6)	- No fatigue	n = 439	168	38.3	33.7–42.8
		- Presence of fatigue		271	61.7	57.2–66.3
Cognition	MMSE (0–30)	- Score ≥ 24 = normal cognition	n = 438	412	94.1	91.9–96.3
		- Score ≤ 23 = mild/severe cognitive decline		26	5.9	3.7–8.1
Depression	GDS-15 (0–15)	- Score 0–4 = not at risk for depression	n = 437	347	79.4	75.6–83.2
		- Score 5–15 = at risk for depression		90	20.6	16.8–24.4
Nutrition	MNA-SF (0–14)	- Score ≥ 12 = normal nutritional status	n = 439	139	31.7	27.3–36.0
		- Score 8–11 = risk of malnutrition		206	46.9	42.3–51.6
		- Score ≤ 7 = malnourished		94	21.4	17.6–25.2

Legend: CI = confidence interval; fTRST = Flemish version of the Triage Risk Screening Tool; GA = Geriatric Assessment; ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; MOB-T = Mobility – Tiredness Test; MMSE = Mini Mental State Examination; GDS = Geriatric Depression Scale; MNA-SF = Mini Nutritional Assessment – Short Form.

Fig. 2. Flow-chart of the evolution of FS on ADL/IADL during follow-up in patients receiving chemotherapy. *Functional decline on ADL = increase of two or more points. **Functional decline on IADL = decrease of one or more points. Legend: FS: Functional Status; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.

progression/relapse vs new diagnosis) (OR:0.59; 95%CI: 0.39–0.90) was the only factor associated with functional decline in IADL.

3.4. Prognostic value of functional impairment/decline in ADL/IADL for overall survival

At the time of data analysis (February 2016), the median survival time was 21.1 months (95%CI: 17.45–26.38; range: 0.1–75.72; n = 439), and 72% of the patients had died. Baseline FS measured by ADL and IADL (dependent versus independent) were both prognostic for OS with logrank p-value 0.009 and 0.003 respectively (n = 439).

Functional decline in ADL showed a strong prognostic value for OS (logrank p-value < 0.0001; Wilcoxon p-value < 0.0001) (see Fig. 3). Functional decline in IADL also showed a prognostic value for OS (logrank p-value 0.100; Wilcoxon p-value 0.043) (see Fig. 3). However, functional decline in ADL had much higher discriminatory power than decline in IADL as suggested by higher HR for OS: HR for ADL (decline versus no decline) was 2.34 (95% CI 1.75–3.12) and for IADL (decline versus no decline) 1.25 (95% CI 0.97–1.61).

In the multivariable Cox regression analysis factors that showed a strong prognostic capacity for OS were: functional decline in ADL, tumor type, MNA-SF and baseline FS by ADL (p-value: <0.0001, <0.0001; 0.004 and 0.010 respectively). The highest discriminatory power were for functional decline in ADL (HR 2.44; 95%CI 1.80–3.31), and for the following combinations with tumor type 'lung versus hematologic

malignancy' and 'lung versus ovarian' with HR 3.11 (95%CI 1.96–4.93) and 2.79 (95%CI 1.66–4.68) respectively (see Table 5).

4. Discussion

In contrast to many previous studies describing baseline FS in older cancer populations [7,24,40–46], this prospective multicenter study focuses on evolution of FS in patients receiving chemotherapy (functional decline versus stable/improvement). Moreover factors associated with functional decline in older (≥ 70 years) patients with cancer receiving chemotherapy were studied.

Our results show that older patients with cancer receiving chemotherapy experience a significant decline in functional capabilities, as indicated by the presence of functional decline in ADL and IADL in 19.9% and 41.3% respectively. This means that older people more often lose IADL than ADL related capacities 2 to 3 months after initiation of chemotherapy. This is understandable, since ADL measures basic functions required to maintain independence at home, while IADL evaluates more complex activities that require cognitive functions necessary to maintain independence [9]. So, they first lose the more complex functions, and to a lesser extent the more basic functions.

Studies describing the evolution of FS and more specifically functional decline in older patients with cancer are scarce and only appeared recently in the literature, which hampers the comparison of our results with other studies. A few other studies have investigated the evolution of FS in older patients with cancer [19,47–49].

Table 3
Functional decline on the individual items of ADL and IADL in patients receiving chemotherapy.

Functional status	Functional decline at 2–3 months on individual items ^a	Patients receiving chemotherapy			
		n	%	95%CI	
ADL	- Bathing	n = 387	67	17.3	13.5–21.1
	- Dressing		67	17.3	13.5–21.1
	- Toilette		45	11.6	8.4–14.8
	- Transfer		32	8.3	5.5–11.0
	- Continence		61	15.8	12.1–19.4
	- Feeding		26	6.7	4.2–9.2
IADL	- Female	n = 228	3	1.3	0–2.8
	- Shopping		54	23.7	18.2–29.2
	- Cooking		64	28.1	22.2–33.9
	- Housekeeping		26	11.4	7.3–15.5
	- Laundry		43	18.9	13.8–23.9
	- Mode of transportation		57	25.0	19.4–30.6
	- Responsibility of own medication	n = 159	28	12.3	8.0–16.5
	- Ability to handle finances		23	10.1	6.2–14.0
	- Male		5	3.1	0.4–5.9
	- Shopping		32	20.1	13.9–26.4
	- Mode of transportation		34	21.4	15.0–27.8
	- Responsibility of own medication		28	17.6	11.7–23.5
	- Ability to handle finances		17	10.7	5.9–15.5

Legend: CI = confidence interval; ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living.

^a Functional decline on individual items on ADL is defined as an increase of one or more points. Functional decline on individual items on IADL is defined as a decrease of one point.

The study of Puts et al. focused on older patients with newly-diagnosed cancer (n = 112; both solid tumors and hematologic malignancies). They included all types of cancer treatment, not only chemotherapy, and showed that 22.0% of patients experienced functional

decline during a six-month follow-up period, not mentioning the results separately for decline in ADL and IADL [19]. Another study, focusing on one year follow-up, describes the presence of functional decline in 58% of older patients with cancer (n = 134; breast and colorectal cancer, stage I–III), again not reporting the results separately for ADL and IADL [49]. The study of Hoppe et al. is focusing on older patients with cancer receiving first-line chemotherapy (n = 364; both solid tumors and non-Hodgkin lymphoma) [47]. They report an observed functional decline in ADL in 16.7% which is slightly lower than in our study (19.9%). This could be related to the fact that in our study patients received chemotherapy in any setting (not only first-line). In the study of Ronning et al., higher rates of functional decline are observed: 31% and 69% for ADL and IADL respectively (n = 84) [48]. Probably the population studied (patients with colorectal cancer undergoing surgery) and the impact of surgery on function explains these high numbers, suggesting that the type of treatment has differential impact on FS.

Overall, these results confirm that functional decline occurs frequently during treatment of older patients with cancer. Nevertheless, it is difficult to draw firm conclusions, because of the differences between the studies concerning tumor types, settings, treatment modalities, follow-up period and measuring instruments used.

Additionally, we did not find any study in the literature describing the evolution of the individual ADL and IADL items after the initiation of chemotherapy. For ADL, we can conclude that the highest impact during chemotherapy treatment is on the items bathing, dressing and continence. For IADL, both female and male patients, the most prominent items for decline are shopping and mode of transportation. For female patients cooking should be added to this list.

Focus on the individual items is important for the development of prevention programs for functional decline and professional health care workers need to pay specific attention to these items to ensure that support can be given during treatment with chemotherapy.

Assessment of FS and determination of factors associated with functional decline are very useful to assist the treating physician in treatment decision making and in identification of individuals at high

Table 4
Factors associated with functional decline on ADL/IADL in patients receiving chemotherapy in univariate and multivariable analysis.

Variable	Categorisation	Functional decline on ADL				Functional decline on IADL			
		Univariate	Multivariable			Univariate	Multivariable		
		p-Value	p-Value	OR	95% CI	p-Value	p-Value	OR	95% CI
Age	70–74 vs 75–79 vs ≥80y	0.603				0.593			
fTRST	Geriatric risk profile (≥1) vs no geriatric risk profile (0)	0.075				0.349			
G8	Geriatric risk profile (≤14) vs no geriatric risk profile (>14)	0.026	–			0.210			
Oncological setting	Progression/relapse vs new diagnosis	0.236				0.014	0.014	0.59	0.39–0.90
ECOG-PS	Score 2–4 vs score 0–1	0.020	–			0.220			
Fall history in the past 12 months	Falls in the past 12 months vs no falls	0.139				0.877			
Pain	Mild pain/pain to treat vs no pain	0.756				0.865			
Polypharmacy	≥5 different drugs vs 0–4 different drugs	0.089				0.147			
Living situation	Living alone vs living with help	0.133				0.108			
CCI	Comorbidities (≥1) vs no comorbidities (0)	0.285				0.938			
ADL	ADL dependent (≥7) vs ADL independent (6)	0.127				0.961			
IADL	IADL dependent (≤4(male)/7(female) vs IADL independent (5(male)/8(female))	0.011	0.037	1.76	1.03–2.99	0.389			
Fatigue by MOB-T	Presence of fatigue vs no fatigue	0.030	–			0.081			
MMSE	Mild/severe cognitive decline (≤23) vs normal cognition (≥24)	0.394				0.089			
GDS-15	At risk for depression (≥5) vs not at risk (0–4)	0.261				0.245			
MNA-SF	Risk for malnutrition/malnourished (≤11) vs normal nutritional status (≥12)	0.008	0.007	2.02	1.10–3.71	0.809			
Surgery	Surgery vs no surgery	0.217				0.370			
Radiotherapy	Radiotherapy vs no radiotherapy	0.335				0.031	–		
Tumor type	Breast vs colorectal vs prostate vs lung vs ovarian vs hematologic malignancies	0.271				0.072			

Legend: y = year; CI = confidence interval; OR = odds ratio; fTRST = Flemish version of the Triage Risk Screening Tool; ECOG-PS = Eastern Cooperative Oncology Group Performance Status; CCI = Charlson Comorbidity Index; ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; MOB-T = Mobility – Tiredness Test; MMSE = Mini Mental State Examination; GDS-15 = 15 item Geriatric Depression Scale; MNA-SF = Mini Nutritional Assessment – Short Form; vs = versus.

Fig. 3. Impact of functional decline measured by ADL and IADL on OS ($n = 387$). Legend: ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living. Overall survival, defined as the time from study entry until death, of older patients with cancer with or without functional decline after 2 to 3 months, measured by ADL and IADL ($n = 387$). Panel A and B show Kaplan Meier estimates of the probability of overall survival with or without functional decline measured by ADL and IADL. Difference between functional decline and no functional decline was evaluated by two-sided logrank test and Wilcoxon's test (data not reported in the figure). Functional decline on ADL (range: 6–24) was defined as an increase of two or more points and functional decline on IADL (range: 0–8 (female); 0–5 (male)) as a decrease of one or more points. ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living.

risk for future disability. Several factors associated with functional decline in ADL and IADL were identified by multivariable analysis.

In our study we found that factors associated with functional decline in ADL were baseline IADL dependency and abnormal nutritional status ($\text{MNA-SF} \leq 11$). In the study of Hoppe et al. baseline IADL dependency was also a factor associated with functional decline in ADL [47]. This suggests that impairments in IADL before initiation of chemotherapy increase the risk of subsequent impairments on ADL. Another important factor associated with functional decline in ADL in our study is nutritional status, which is in accordance with other studies in the general older

population [50,51]. The only factor associated with functional decline in IADL was the oncological setting (disease progression/relapse vs new diagnosis). Patients included with a new diagnosis seem to have more risk for functional decline in IADL than patients included at disease progression/relapse. This could be explained by the possibility that patients with disease progression/relapse already experienced functional decline during previous therapy.

Looking at the factors that were not associated with functional decline in ADL and IADL in our study, we can conclude that age is one of them. Hoppe et al. already stated that this factor in particular has been

Table 5
Results of the multivariable Cox regression analysis for overall survival.

Variable		Logrank p-value	Hazard ratio	95%CI
Functional decline in ADL	Decline vs no decline	<0.0001	2.44	1.80–3.31
Tumor type	Breast vs lung	<0.0001	0.31	0.19–0.51
	Breast vs colorectal		0.54	0.37–0.81
	Breast vs ovarian		0.86	0.52–1.43
	Breast vs prostate		0.38	0.21–0.70
	Breast vs hematologic malignancy		0.97	0.63–1.49
	Lung vs colorectal		1.75	1.14–2.70
	Lung vs ovarian		2.79	1.66–4.68
	Lung vs prostate		1.23	0.65–2.31
	Lung vs hematologic malignancy		3.11	1.96–4.93
	Colorectal vs ovarian		1.59	1.02–2.49
	Colorectal vs prostate		0.70	0.40–1.24
	Colorectal vs hematologic malignancy		1.78	1.22–2.58
	Ovarian vs prostate		0.44	0.23–0.84
	Ovarian vs hematologic malignancy		1.12	0.70–1.78
	Prostate vs hematologic malignancy		2.54	1.41–4.58
MNA-SF	Normal nutritional status (≥ 12) vs at risk for malnutrition/malnourished (≤ 11)	0.004	0.65	0.48–0.89
ADL	ADL independent (6) vs ADL dependent (≥ 7)	0.010	0.71	0.54–0.92

Legend: ADL = Activities of Daily Living; MNA-SF = Mini Nutritional Assessment – Short Form; CI = confidence interval; vs = versus.

highlighted as an independent factor in studies in the general older population [47,52,53], but neither in the study of Hoppe et al. nor in our study this was observed in the older population with cancer. This supports the heterogeneity of the aging process and highlights the importance of the implementation of CGA including assessment of FS when treating older patients with cancer.

Secondly, it should be acknowledged that several factors associated with functional decline described in univariate analysis, were not identified as factors associated with functional decline in ADL or IADL in older patients with cancer by multivariable analysis in the current study, meaning that more factors are influencing functional decline but with smaller impact.

To our knowledge, the prognostic value of functional decline for OS in older patients with cancer, whether or not receiving chemotherapy, has not been studied before. Most but not all studies, identified baseline GA components as independent factors to predict OS [7] and baseline FS is one of the most consistent factors associated with OS in older patients with cancer, and more specifically IADL status. [7,44,45,54,55] This was also confirmed in our cohort with mature data. To determine the prognostic value of functional decline after the initiation of chemotherapy, we performed a Cox proportional hazard regression with functional decline in ADL and IADL separately as the independent variables, and a multivariable Cox regression. Functional decline in ADL and IADL at 2 to 3 months after initiation of chemotherapy were both prognostic for OS with the highest discriminatory power for functional decline in ADL. In the multivariable Cox regression functional decline in ADL had also the highest prognostic value for OS. Although older patients with cancer experience more frequently a functional decline in IADL, the effect of functional decline in ADL has a stronger impact on the general health status with higher mortality as consequence. Functional decline in ADL is thus less prevalent than IADL decline, but has more impact on survival. Additionally, we can also state that having impairments on IADL at baseline has more impact on OS than experiencing functional decline in IADL. The contrary is true for ADL dependency and functional decline in ADL.

This study has some limitations. First, there is no current consensus on the criteria to define functional decline related to the instrument that is used to measure ADL (e.g. Katz's scale or Barthel Index) and over which period it should be monitored [23,49,56]. Secondly, we included a quite heterogeneous population, where the setting (early versus advanced diseases), tumor type (6 tumor types with each type consisting of sometimes very different subtypes), and the choice of chemotherapy regimen can have different impact on FS, functional decline and OS. Strengths of the study are the fact that both ADL and IADL are integrated and investigated, the subanalysis of the individual

components of these scales, the use of a prospective multicentric design and a low drop-out rate.

5. Conclusions

In conclusion, this study shows that functional decline occurs frequently in older patients with cancer receiving chemotherapy, and is even more pronounced for IADL than for ADL activities. GA components (IADL and MNA-SF) are identified as independent factors associated with functional decline in ADL during chemotherapy treatment. Functional decline in IADL was mainly seen in patients with a new cancer diagnosis. Additionally, functional decline, especially decline in ADL, has a strong prognostic value for OS. Focus on the individual ADL and IADL items should support the development and implementation of interventions preventing functional decline in patients at risk during chemotherapy treatment.

Disclosures and conflict of interest statement

The authors declare that they have no competing interests.

Author contributions

Study Concepts: C Kenis, L Decoster, Johan Flamaing, K Milisen, H Wildiers.

Study Design: C Kenis, L Decoster, J Bastin, H Bode, K Van Puyvelde, J De Grève, G Conings, K Fagard, Johan Flamaing, K Milisen, JP Lobelle, H Wildiers.

Data Acquisition: C Kenis, L Decoster.

Quality Control of Data and Algorithms: C Kenis, L Decoster, JP Lobelle, H Wildiers.

Data Analysis and Interpretation: C Kenis, L Decoster, Johan Flamaing, K Milisen, JP Lobelle, H Wildiers.

Statistical Analysis: JP Lobelle.

Manuscript Preparation: C Kenis, H Wildiers.

Manuscript Editing: C Kenis, L Decoster, J Bastin, H Bode, K Van Puyvelde, J De Grève, G Conings, K Fagard, Johan Flamaing, K Milisen, JP Lobelle, H Wildiers.

Manuscript Review: C Kenis, L Decoster, J Bastin, H Bode, K Van Puyvelde, J De Grève, G Conings, K Fagard, Johan Flamaing, K Milisen, JP Lobelle, H Wildiers.

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Appendix A. Evolution of functional status related to tumor type

		ADL evolution (n = 387)		
		Improvement n (%)	Stable n (%)	Decline n (%)
Breastcancer (n = 95)		11 (11.58)	66 (69.47)	18 (18.95)
Colorectal cancer (n = 95)		16 (16.85)	64 (67.37)	15 (15.79)
Prostate cancer (n = 16)		3 (18.75)	12 (75.00)	1 (6.25)
Ovarian cancer (n = 43)		5 (11.63)	25 (58.14)	13 (30.23)
Lungcancer (n = 38)		0 (0)	28 (73.68)	10 (26.32)
Hematologic malignancy (n = 100)		9 (9.00)	71 (71.00)	20 (20.00)

		IADL evolution (n = 387)		
		Improvement n (%)	Stable n (%)	Decline n (%)
Breastcancer (n = 95)		21 (22.11)	28 (29.47)	46 (48.42)
Colorectal cancer (n = 95)		17 (17.90)	50 (52.63)	28 (29.47)
Prostate cancer (n = 16)		3 (18.75)	8 (50.00)	5 (31.25)
Ovarian cancer (n = 43)		12 (27.91)	12 (27.91)	19 (44.19)
Lungcancer (n = 38)		4 (10.53)	14 (36.84)	20 (52.63)
Hematologic malignancy (n = 100)		15 (15.00)	43 (43.00)	42 (42.00)

Legend: ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living.

Appendix B. Evolution of functional status related to tumor type and staging of the tumor

		ADL evolution (n = 387)		
		Improvement n (%)	Stable n (%)	Decline n (%)
Breastcancer (n = 95)	Stage I (n = 2)	0 (0)	2 (2.11)	0 (0)
	Stage II (n = 26)	4 (4.21)	20 (21.05)	2 (2.11)
	Stage III (n = 20)	2 (2.11)	14 (14.74)	4 (4.21)
	Stage IV (n = 47)	5 (5.26)	30 (31.58)	12 (12.63)
Colorectal cancer (n = 95)	Stage I (n = 1)	0 (0)	1 (1.05)	0 (0)
	Stage II (n = 5)	1 (1.05)	4 (4.21)	0 (0)
	Stage III (n = 12)	1 (1.05)	8 (8.42)	3 (3.16)
	Stage IV (n = 77)	14 (14.74)	51 (53.68)	12 (12.63)
Prostate cancer (n = 16)	Stage I (n = 0)	0 (0)	0 (0)	0 (0)
	Stage II (n = 0)	0 (0)	0 (0)	0 (0)
	Stage III (n = 0)	0 (0)	0 (0)	0 (0)
	Stage IV (n = 3)	3 (18.75)	12 (75.00)	1 (6.25)
Ovarian cancer (n = 43)	Stage I (n = 2)	2 (4.65)	0 (0)	0 (0)
	Stage II (n = 1)	0 (0)	0 (0)	1 (2.33)
	Stage III (n = 20)	2 (4.65)	13 (30.23)	5 (11.63)
	Stage IV (n = 20)	1 (2.33)	12 (27.91)	7 (16.28)
Lungcancer (n = 38)	Stage I (n = 0)	0 (0)	0 (0)	0 (0)
	Stage II (n = 1)	0 (0)	1 (2.63)	0 (0)
	Stage III (n = 7)	0 (0)	7 (18.42)	0 (0)
	Stage IV (n = 30)	0 (0)	20 (52.63)	10 (26.32)
Hematologic malignancy (n = 100)		9 (9.00)	71 (71.00)	20 (20.00)

		IADL evolution (n = 387)		
		Improvement n (%)	Stable n (%)	Decline n (%)
Breastcancer (n = 95)	Stage I (n = 2)	0 (0)	2 (2.11)	0 (0)
	Stage II (n = 26)	5 (5.26)	8 (8.42)	13 (13.68)
	Stage III (n = 20)	4 (4.21)	4 (4.21)	12 (12.63)
	Stage IV (n = 47)	12 (12.63)	14 (14.74)	21 (22.11)

Appendix B (continued)

		IADL evolution (n = 387)		
		Improvement n (%)	Stable n (%)	Decline n (%)
Colorectal cancer (n = 95)	Stage I (n = 1)	1 (1.05)	0 (0)	0 (0)
	Stage II (n = 5)	3 (3.16)	2 (2.11)	0 (0)
	Stage III (n = 12)	2 (2.11)	7 (51.58)	3 (3.16)
	Stage IV (n = 77)	11 (11.58)	41 (43.16)	25 (26.32)
Prostate cancer (n = 16)	Stage I (n = 0)	0 (0)	0 (0)	0 (0)
	Stage II (n = 0)	0 (0)	0 (0)	0 (0)
	Stage III (n = 0)	0 (0)	0 (0)	0 (0)
	Stage IV (n = 3)	3 (18.75)	8 (50.00)	5 (31.25)
Ovarian cancer (n = 43)	Stage I (n = 2)	0 (0)	0 (0)	2 (4.65)
	Stage II (n = 1)	0 (0)	0 (0)	1 (2.33)
	Stage III (n = 20)	5 (11.63)	7 (16.28)	8 (18.60)
	Stage IV (n = 20)	7 (16.28)	5 (11.63)	8 (18.60)
Lungcancer (n = 38)	Stage I (n = 0)	0 (0)	0 (0)	0 (0)
	Stage II (n = 1)	1 (2.63)	0 (0)	0 (0)
	Stage III (n = 7)	0 (0)	4 (10.53)	3 (7.89)
	Stage IV (n = 30)	3 (7.89)	10 (26.32)	17 (44.74)
Hematologic malignancy (n = 100)		15 (15.00)	43 (43.00)	42 (42.00)

Legend: ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living.

References

- [1] Burhenn PS, McCarthy AL, Begue A, Nightingale G, Cheng K, Kenis C. Geriatric assessment in daily oncology practice for nurses and allied health care professionals: Opinion paper of the Nursing and Allied Health Interest Group of the International Society of Geriatric Oncology (SIOG). *J Geriatr Oncol* 2016;7(5):315–24.
- [2] Repetto L, Fratio L, Audisio RA, Venturino A, Gianni W, Vercelli M, et al. Comprehensive geriatric assessment adds information to Eastern Cooperative Oncology Group performance status in elderly cancer patients: an Italian Group for Geriatric Oncology Study. *J Clin Oncol* 2002;20(2):494–502.
- [3] Wedding U, Rohrig B, Klippstein A, Pientka L, Hoffken K. Age, severe comorbidity and functional impairment independently contribute to poor survival in cancer patients. *J Cancer Res Clin Oncol* 2007;133(12):945–50.
- [4] Jordhoy MS, Fayers P, Loge JH, Saltnes T, Ahlner-Elmqvist M, Kaasa S. Quality of life in advanced cancer patients: the impact of sociodemographic and medical characteristics. *Br J Cancer* 2001;85(10):1478–85.
- [5] Yates JW, Chalmer B, McKegney FP. Evaluation of patients with advanced cancer using the Karnofsky performance status. *Cancer* 1980;45(8):2220–4.
- [6] Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, Mcfadden ET, et al. Toxicity and response criteria of the Eastern-Cooperative-Oncology-Group. *Am J Clin Oncol Cancer Clin Trials* 1982;5(6):649–55.
- [7] Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol* 2014;32(24):2595–603.
- [8] Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA* 1963;185:914–9.
- [9] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9(3):179–86.
- [10] Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment – a metaanalysis of controlled trials. *Lancet* 1993;342(8878):1032–6.
- [11] Pallis AG, Wedding U, Lacombe D, Soubeyran P, Wildiers H. Questionnaires and instruments for a multidimensional assessment of the older cancer patient: what clinicians need to know? *Eur J Cancer* 2010;46(6):1019–25.
- [12] Rubenstein LZ, Stuck AE, Siu AL, Wieland D. Impacts of geriatric evaluation and management programs on defined outcomes: overview of the evidence. *J Am Geriatr Soc* 1991;39(9 Pt 2):85–165 [discussion 75–85].
- [13] Hoogerduijn JG, Schuurmans MJ, Korevaar JC, Buurman BM, de Rooij SE. Identification of older hospitalised patients at risk for functional decline, a study to compare the predictive values of three screening instruments. *J Clin Nurs* 2010;19(9–10):1219–25.
- [14] Covinsky KE, Justice AC, Rosenthal GE, Palmer RM, Landefeld CS. Measuring prognosis and case mix in hospitalized elders. The importance of functional status. *J Gen Intern Med* 1997;12(4):203–8.
- [15] Fortinsky RH, Covinsky KE, Palmer RM, Landefeld CS. Effects of functional status changes before and during hospitalization on nursing home admission of older adults. *J Gerontol A Biol Sci Med Sci* 1999;54(10):M521–6.
- [16] Rudberg MA, Sager MA, Zhang J. Risk factors for nursing home use after hospitalization for medical illness. *J Gerontol A Biol Sci Med Sci* 1996;51(5):M189–94.
- [17] McCormick RE. Possible acceleration of aging by adjuvant chemotherapy: a cause of early onset frailty? *Med Hypotheses* 2006;67(2):212–5.
- [18] Versteeg KS, Konings IR, Lagaay AM, van de Loosdrecht AA, Verheul HM. Prediction of treatment-related toxicity and outcome with geriatric assessment in elderly patients with solid malignancies treated with chemotherapy: a systematic review. *Ann Oncol* 2014;25(10):1914–8.
- [19] Puts MTE, Monette J, Girre V, Wolfson C, Monette M, Batist G, et al. Changes in functional status in older newly-diagnosed cancer patients during cancer treatment:

- a six-month follow-up period. Results of a prospective pilot study. *J Geriatr Oncol* 2011;2(2):112–20.
- [20] Balducci L, Stanta G. Cancer in the frail patient. A coming epidemic. *Hematol Oncol Clin North Am* 2000;14(1):235–50 [xi].
 - [21] Arnold M, Karim-Kos HE, Coebergh JW, Byrnes G, Antilla A, Ferlay J, et al. Recent trends in incidence of five common cancers in 26 European countries since 1988: analysis of the European cancer observatory. *Eur J Cancer* 2015;51(9):1164–87.
 - [22] Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: burdens upon an aging, changing nation. *J Clin Oncol* 2009;27(17):2758–65.
 - [23] McCusker J, Kakuma R, Abrahamowicz M. Predictors of functional decline in hospitalized elderly patients: a systematic review. *J Gerontol A Biol Sci Med Sci* 2002;57(9):M569–77.
 - [24] Kenis C, Decoster L, Van Puyvelde K, De Greve J, Conings G, Milisen K, et al. Performance of two geriatric screening tools in older patients with cancer. *J Clin Oncol* 2014;32(1):19–26.
 - [25] Braes T, Flamaing J, Sterckx W, Lipkens P, Sabbe M, de Rooij SE, et al. Predicting the risk of functional decline in older patients admitted to the hospital: a comparison of three screening instruments. *Age Ageing* 2009;38(5):600–3.
 - [26] Meldon SW, Mion LC, Palmer RM, Drew BL, Connor JT, Lewicki LJ, et al. A brief risk-stratification tool to predict repeat emergency department visits and hospitalizations in older patients discharged from the emergency department. *Acad Emerg Med* 2003;10(3):224–32.
 - [27] Soubeyran P, Bellera C, Goyard J, Heitz D, Cure H, Rousselot H, et al. Validation of the G8 screening tool in geriatric oncology: the ONCODAGE project. ASCO annual meeting 2011; Chicago. *J Clin Oncol* 2011;29 (suppl; abstr 9001).
 - [28] Bellera CA, Rainfray M, Mathoulin-Pelissier S, Mertens C, Delva F, Fonck M, et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. *Ann Oncol* 2012;23(8):2166–72.
 - [29] Lamb SE, Jorstad-Stein EC, Hauer K, Becker C. Development of a common outcome data set for fall injury prevention trials: the prevention of Falls Network Europe consensus. *J Am Geriatr Soc* 2005;53(9):1618–22.
 - [30] Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988;319(26):1701–7.
 - [31] 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.
 - [32] Yesavage JA, 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):37–49.
 - [33] Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* 2001;56(6):M366–72.
 - [34] Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bannahum D, Lauque S, et al. The mini nutritional assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition* 1999;15(2):116–22.
 - [35] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40(5):373–83.
 - [36] Avlund K, Holstein BE. Functional ability among elderly people in three service settings: the discriminatory power of a new functional ability scale. *Eur J Epidemiol* 1998;14(8):783–90.
 - [37] Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain* 1997;72(1–2):95–7.
 - [38] Deschodt M, Wellens NI, Braes T, De VA, Boonen S, Flamaing J, et al. Prediction of functional decline in older hospitalized patients: a comparative multicenter study of three screening tools. *Aging Clin Exp Res* 2011;23(5–6):421–6.
 - [39] Geyskens K, De RK, Sabbe M, Braes T, Milisen K, Flamaing J, et al. Prediction of functional decline in elderly patients discharged from the accident and emergency department. *Tijdschr Gerontol Geriatr* 2008;39(1):16–25.
 - [40] Aliamur V, Adam C, Druet-Cabanac M, Dantoine T, Vergnenegre A. Geriatric assessment contribution to treatment decision-making in thoracic oncology. *Rev Mal Respir* 2011;28(9):1124–30.
 - [41] Hamaker ME, Vos AG, Smorenburg CH, de Rooij SE, van Munster BC. The value of geriatric assessments in predicting treatment tolerance and all-cause mortality in older patients with cancer. *Oncologist* 2012;17(11):1439–49.
 - [42] Kenis C, Bron D, Libert Y, Decoster L, Van Puyvelde K, Scalliet P, et al. Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicenter study. *Ann Oncol* 2013;24(5):1306–12.
 - [43] Klepin HD, Geiger AM, Tooze JA, Kritchevsky SB, Williamson JD, Ellis LR, et al. The feasibility of inpatient geriatric assessment for older adults receiving induction chemotherapy for acute myelogenous leukemia. *J Am Geriatr Soc* 2011;59(10):1837–46.
 - [44] Maione P, Perrone F, Gallo C, Manzione L, Piantadosi F, Barbera S, et al. Pretreatment quality of life and functional status assessment significantly predict survival of elderly patients with advanced non-small-cell lung cancer receiving chemotherapy: a prognostic analysis of the multicenter Italian lung cancer in the elderly study. *J Clin Oncol* 2005;23(28):6865–72.
 - [45] Puts M, Hardt J, Monette J, Girre V, Springall E, Alibhai SM. A systematic review of the use of geriatric assessment for older adults in oncology. *Gerontologist* 2012;52:629.
 - [46] Soubeyran P, Fonck M, Blanc-Bisson C, Blanc JF, Ceccaldi J, Mertens C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. *J Clin Oncol* 2012;30(15):1829–34.
 - [47] Hoppe S, Rainfray M, Fonck M, Hoppenreys L, Blanc JF, Ceccaldi J, et al. Functional decline in older patients with cancer receiving first-line chemotherapy. *J Clin Oncol* 2013;31(31):3877–82.
 - [48] Ronning B, Wyller TB, Jordhoy MS, Nesbakken A, Bakka K, Seljeflot I, et al. Frailty indicators and functional status in older patients after colorectal cancer surgery. *J Geriatr Oncol* 2014;5(1):26–32.
 - [49] Deckx L, van den Akker M, Daniels L, De Jonge ET, Bulens P, Tjan-Heijnen VC, et al. Geriatric screening tools are of limited value to predict decline in functional status and quality of life: results of a cohort study. *BMC Fam Pract* 2015;16:30.
 - [50] Dent E, Visvanathan R, Piantadosi C, Chapman I. Nutritional screening tools as predictors of mortality, functional decline, and move to higher level care in older people: a systematic review. *J Nutr Gerontol Geriatr* 2012;31(2):97–145.
 - [51] Kiesswetter E, Pohlhausen S, Uhlig K, Diekmann R, Lesser S, Uter W, et al. Prognostic differences of the mini nutritional assessment short form and long form in relation to 1-year functional decline and mortality in community-dwelling older adults receiving home care. *J Am Geriatr Soc* 2014;62(3):512–7.
 - [52] Covinsky KE, Palmer RM, Fortinsky RH, Counsell SR, Stewart AL, Kresevic D, et al. Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: increased vulnerability with age. *J Am Geriatr Soc* 2003;51(4):451–8.
 - [53] Cornette P, Swine C, Malhomme B, Gillet JB, 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.
 - [54] Freyer G, Geay JF, Touzet S, Provencal J, Weber B, Jacquin JP, et al. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. *Ann Oncol* 2005;16(11):1795–800.
 - [55] Gironés R, Torregrosa D, Maestu I, Gómez-Codina J, Tenias JM, Costa RR. Comprehensive geriatric assessment (CGA) of elderly lung cancer patients: a single-center experience. *J Geriatr Oncol* 2012;3(2):98–103.
 - [56] 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.