The incremental value of a geriatric assessment-derived three-item scale on estimating overall survival in older adults with cancer

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ABSTRACT

Objective: A geriatric assessment (GA) assesses functional age of older patients with cancer and is a well-established tool predictive of toxicity and survival. The objective of this study was to investigate the prognostic value of individual GA items.
Materials and Methods: 546 patients with cancer ≥ 65 years completed GA from 2009 to 2014 and were followed for survival status for a median of 3.7 years. The GA consisted of function, nutrition, comorbidity, cognition, psychological state, and social activity/support domains. GA items with $p < 0.05$ in univariable analyses for overall survival (OS) were entered into multivariable stepwise selection procedure using a Cox proportional hazards model. A prognostic scale was constructed with significant GA items retained in the final model.
Results: Median age was 72 years, 49% had breast cancer, and 42% had stage 3–4 cancer. Three GA items were significant prognostic factors, independent of traditional factors (cancer type, stage, age, and Karnofsky Performance Status): (1) "limitation in walking several blocks", (2) "limitation in shopping", and (3) "≥ 5% unintentional weight loss in 6 months". A three-item prognostic scale was constructed with these items. In comparison with score 0 (no positive items), hazard ratios for OS were 1.85 for score 1, 2.97 for score 2, and 8.67 for score 3. This translated to 2-year estimated survivals of 85%, 67%, 51% and 17% for scores of 0, 1, 2 and 3, respectively.
Conclusions: This three-item scale was a strong independent predictor of survival. If externally validated, this could be a streamlined tool with broader applicability.

1. Introduction

An accurate estimate of overall survival is essential for shared decision-making between patients with cancer and clinicians. Survival of patients with cancer is typically estimated based on cancer type, disease stage and oncology performance status measures, such as Karnofsky Performance Status (KPS) or Eastern Cooperative Oncology Group (ECOG) performance status, regardless of age [1,2]. A concern is that these performance status measures do not address the heterogeneity in health status of older adults with cancer [3]. Geriatric assessment (GA) is a helpful tool to identify multidimensional impairments in older patients which are potentially associated with adverse outcomes (i.e., treatment-related toxicities, postoperative complications and functional decline) and survival [4]. The routine use of GA in older adults with cancer is recommended by the International Society of Geriatric Oncology (SIOG) and U.S. National Comprehensive Cancer Network (NCCN); however, there is no consensus on a standard GA tool [5,6]. Partially because of differences in the GA tools used in various studies, the GA variables identified as prognostic for survival have not been consistent across studies [7–10]. Further, the prognostic value of individual items in each GA domain has not been elucidated as most prior studies have focused on associations between GA domains and survival.

In the U.S., the cancer-specific GA developed by Hurria et al. has been the most studied, and its feasibility and utility in routine practice and clinical trials has been demonstrated [11–14]. Using this particular GA, a "chemotherapy toxicity risk score" (CTRS) for older adults with patients receiving chemotherapy was developed and validated [15,16]. Building on prior CTRS research, the aim of this study was to evaluate the prognostic value of individual items in the cancer-specific GA for survival, independent of traditional factors such as cancer type, disease stage, treatment, age, and performance status. Prognostic factors identified as significant were used to construct a scale to predict survival in older adults with cancer.

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2. Methods

2.1. Patient Population

The "Carolina Senior Registry" (CSR) is a cross-sectional study of patients with cancer 65 years or older who completed a cancer-specific GA regardless of cancer type, stage or treatment status (CSR; ClinicalTrials.gov identifier NCT01137825); the sample method is a non-probability sampling [13]. Informed consent had been obtained from all patients prior to participation in the Registry. Eligibility was restricted to patients able to speak and read English. For the present study, we limited analysis to 546 patients in the CSR who were recruited at the North Carolina Cancer Hospital, a large academic medical center, between October 2009 and September 2014 and whose records were linked to the North Carolina Central Cancer Registry (NCCCR) [17]. Survival status was determined through linking to the National Death Index, Social Security Death Index, and North Carolina State Center for Vital Statistics, and was available through August 2015. The patients who remained alive on August 31, 2015, were censored. The NCCCR collects data on all cancers diagnosed in the state of North Carolina including date of diagnosis, cancer type, stage, all-cause and cancer-specific mortality. If there were unspecified cancer-related variables (e.g. cancer type and stage) in the dataset, medical records were reviewed for clarification. Treatment data were extracted from medical records and summarized as curative or palliative intent treatment. The study protocol was approved by the UNC Institutional Review Board.

2.2. Cancer-specific Geriatric Assessment (GA)

The cancer-specific GA used in the CSR was developed by Hurria et al. and is comprised of validated measures [11]. The section of the GA completed by a health-care professional (clinical staff or research assistant) includes the following measures: Karnofsky Performance Status (KPS), Timed Up and Go (TUG) test, Blessed Orientation Memory Concentration (BOMC) test, and Body Mass Index (BMI). Measures that are completed by a patient include: Activities of Daily Living (ADL, subscale of Medical Outcomes Study (MOS) Physical Health), Instrumental Activities of Daily Living (IADL, subscale of the Older American Resources and Services (OARS)), falls, vision, hearing, comorbidities, medications, nutrition, psychological state (Mental Health Inventory-17 (MHI-17)), and social support/function (MOS Social Activity/Social Support Survey).

2.3. Statistical Analysis

Patient and tumor characteristics and geriatric assessment results were summarized descriptively. The primary outcome was overall survival (OS) measured from the date of completion of the GA to date of death. Survival was estimated using the Kaplan Meier method and survival curves were compared using the log rank test.

We ran univariable Cox proportional hazards models to identify variables significantly associated with OS ($p < 0.05$). Individual GA items were dichotomized at the median or at a previously reported cut-off value [15,18]. Variables significant in the univariable analyses were selected for inclusion in a multivariable backward stepwise selection procedure, with a removal criterion of $p > 0.05$ and an entry criterion of $p < 0.025$. To address the potential for collinearity, correlations between all univariable significant items were assessed using Cramer's V; values > 0.50 were considered strong collinearity [9,19]. When there was strong correlation between two variables, the variable with the best Akaike information criterion (AIC) value was entered into the stepwise selection procedure. We included cancer type, stage, treatment, age and KPS to models, as these are traditional factors known to be associated with mortality. The treatment variable was categorical (curative or palliative intent treatment). Because the GA was administered to participants at varying times from diagnosis, time from diagnosis to completion of the GA was also included as a covariate. For sensitivity analysis, we repeated the variable selection procedure using forward stepwise selection.

A prognostic scale was constructed with variables retained in the final stepwise model. The final model was internally validated by calculating the 95% confidence intervals (CIs) for hazard ratios and C-statistic using a nonparametric bootstrap method with 1000 unrestricted random samples. The incremental value of the prognostic scale was assessed by comparing the C-statistic of a model using traditional factors only and then adding the prognostic scale to the traditional factors. We also used the net classification improvement (NRI) proposed by Pencina et al. as a further measure for quantifying the added value from the new predictors [20]. The NRI provides a more rigorous statistical approach to quantifying the correctness of reclassification or movement of predicted probabilities as a result of adding a new variable into prediction models. We used the NRI to evaluate the additive prognostic value of the scale for all-cause mortality at 1 and 2 years [21]. Calibration plots were used to evaluate the performance characteristics of the prognostic scale [22].

As there were differences among patients in time from diagnosis to completion of the GA, an exploratory subgroup analysis was performed with 179 patients who completed the GA within 3 months of their date of diagnosis (incident cancer group). We assessed the prognostic value of the scale for cancer-specific survival. Finally, we performed a subgroup analysis in patients with breast cancer as approximately 50% of patients had breast cancer in this cohort and an exploratory analysis stratified by the treatment variable (curative vs palliative).

Analyses were performed using Stata 14 software (College Station, TX: StataCorp LP) and the R package ("survIDINRI" and 'rms').

3. Results

3.1. Patient Characteristics

From October 2009 to September 2014, 703 patients age ≥ 65 years with various types of cancer were enrolled in the CSR. Of the 703 patients, 546 patients had adequate GA, tumor-specific and survival data [17]. Among the 546 patients included in our analysis, the median age of the study population was 72 years at the time of the GA (range, 65 to 100 years), and 72% of patients were female. The most common type of cancer was breast cancer (49%) and 42% of patients had a stage 3–4 cancer. Most patients had a physician-rated KPS of 80 or greater (81%), with a range of 30 to 100. More detailed patients' characteristics are shown in Table 1. The baseline characteristics of the 157 patients excluded in the process of the data linkage were similar to those included in the final dataset based on bivariable analyses: median age 73 years ($p = 0.30$), 67% female ($p = 0.20$), 87% white ($p = 0.69$), 45% breast cancer ($p = 0.32$) and 78% physician-rated KPS ≥ 80 ($p = 0.44$).

3.2. Geriatric Assessment Results

In total, 39% patients had a MOS-ADL score lower than 70, with a higher score indicating better physical capacity (Table 2). Thirty-seven percent of patients reported impairment in at least one IADL and 24% had at least one fall in the last 6 months. Unintentional weight loss ≥ 5% in the past 6 months was reported in 22% of patients. The median number of comorbidities and prescribed medications were two and five, respectively. Five percent of patients had abnormalities in cognition on the BOMC test.

3.3. Univariable Survival Analysis

The median time since the GA was conducted was 3.7 years (range 0.9 to 5.7 years). 191 patients died from any cause, with an overall 1-year risk of mortality of 20%. 143 deaths (74.9%) were attributable to cancer. Cancer-related factors (cancer type, stage and treatment

Table 1
Patient characteristics.

Characteristic	No. of patients (N = 546)	% patients
Age, years		
65–69	208	38
70–74	155	28
75–79	91	17
≥80	92	17
Sex		
Female	393	72
Male	153	28
Cancer type		
Breast	268	49
Lung and bronchus	73	13
Hematologic malignancy	68	12
Gastrointestinal	48	9
Genitourinary	38	7
Head and neck	26	5
Other	25	5
Cancer stage		
Stage I	165	30
Stage II	142	26
Stage III	106	19
Stage IV	125	23
Unstaged/unknown	8	1
Physician-rated KPS		
100	151	28
80–90	285	53
60–70	90	17
≤50	15	3
Educational level		
HS graduate or less	267	49
Associate/bachelor's	150	28
Advanced degree	126	23
Race		
White	463	85
Other	83	15
Time from diagnosis to complete GA		
≤3 months	179	33
3 months to 18 months	154	28
>18 months	213	39
Treatment intent		
Curative	378	69
Palliative	168	31

Abbreviations: GA, geriatric assessment; KPS, Karnofsky Performance Status.

Table 2
Results of the geriatric assessments.

GA variable	Total (N = 546)
Functional status	
MOS-ADL, mean (SD)	68.2 (28.8)
<70, no. (%)	213 (39)
IADL, mean (SD)	12.9 (2.0)
<14, no. (%)	197 (37)
Falls, mean (SD)	0.5 (1.5)
≥1, no. (%)	129 (24)
TUG, mean (SD)	12.0 (4.8)
Median (IQR)	11.9 (9.6–15.9)
Nutritional status	
Body Mass Index, mean (SD)	27.4 (5.7)
Median (IQR)	26.6 (23.3–30.1)
Percent unintentional weight loss in last 6 months, mean (SD)	3.1 (6.1)
≥5%, no. (%)	122 (22)
Comorbidity	
No. of comorbid conditions, mean (SD)	2.7 (1.8)
Median (IQR)	2 (1–4)
Polypharmacy	
No. of total medication, mean (SD)	8.0 (4.4)
Median (IQR)	8 (5–10)
No. of prescribed medication, mean (SD)	5.3 (3.4)
Median (IQR)	5 (3–7)
Cognition	
BOMC, mean (SD)	4.1 (4.0)
≥11, no. (%)	28 (5)
Psychologic state	
MHI-17, mean (SD)	82.5 (12.7)
Median (IQR)	84.7 (75.3–91.8)
Social support	
MOS-social activity survey, mean (SD)	63.1 (20.8)
Median (IQR)	68.8 (50.0–75.0)
MOS-Social Support Survey, mean (SD)	85.8 (19.3)
Median (IQR)	95.8 (77.1–100)

Abbreviations: ADL, Activities of Daily Living; BOMC, Blessed Orientation Memory Concentration test; IADL, Instrumental Activities of Daily Living; IQR, interquartile range; MHI-17, Mental Health Inventory-17; MOS, Medical Outcomes Study; SD, standard deviation; TUG, Timed Up and Go test.

intent) and traditional patient-related factors (age, and performance status) were prognostic of OS. GA items significantly associated with OS are summarized in Table 3 and came from the following GA domains; functional status (MOS-ADL, IADL, TUG, visual and hearing impairments), nutrition, comorbidity, polypharmacy, cognition, psychologic state and MOS Social Activity. We assessed polypharmacy with two different cut-off values; ">3 prescription drugs" (HR 1.30, 95% CI; 0.90–1.87, p = 0.17) and "≥5 prescription drugs" (HR 1.46, 95% CI; 1.08–1.98, p = 0.013), respectively based on the previous publication [23] and the median value of this cohort.

3.4. Multivariable Survival Analysis

Thirty four GA items were significant prognostic variables based on the univariable survival analyses. Eleven variables were not entered into the stepwise selection procedure because of collinearity. A strong correlation was seen mainly among the MOS-ADL and IADL items (summarized in Supplementary Table 1). We also found a strong correlation between cancer stage and treatment intent (Cramer's V > 0.5). Thus, we built two separate stepwise variable selection models; "stage model" adjusting for cancer stage, type, age, KPS, and time from diagnosis to GA completion and "treatment model" adjusting for treatment intent, cancer type, age, KPS, and time from diagnosis to GA completion. Using the backward stepwise selection procedure, three GA items emerged as independently significant prognostic variables in both the "stage" and "treatment" models (Supplementary Table 2). These items were: (1) "limitation in walking several blocks" from MOS-ADL, (2) "limitation in shopping" from IADL, and (3) "≥5% unintentional weight loss in 6 months" from nutrition domain. Sensitivity analysis using the forward stepwise selection procedure resulted in the same three variables. The "stage" model had a better fit than the "treatment" model based on lower AIC and we adjusted the subsequent models for cancer stage, type, age, KPS, and time from diagnosis to GA completion.

3.5. Development of Three-item Prognostic Scale

We constructed a prognostic scale using the three independently significant prognostic factors for OS identified through the stepwise selection procedure. This three-item scale was used to define four prognostic categories (Fig. 1). Setting a group of patients with no deficits as a reference, the HR for mortality was 1.85 (95% CI 1.25–2.74) for patients with one deficit, 2.97 (95% CI 1.84–4.78) for patents with two deficits, and 8.67 (95% CI 4.97–15.15) for patients with three deficits (Table 4). This translated to 2-year estimated survivals of 85%, 67%, 51% and 17% for patients with zero, one, two and three deficits, respectively (Fig. 1). An increment in the C-statistic was observed when the three-item scale was added to the traditional model comprised of cancer type, stage, age, and KPS: 0.76 (95% CI; 0.73–0.79) for the traditional model and 0.80 (95% CI; 0.77–0.83) for the addition of the three-item scale. Compared to the model using just traditional prognostic factors, the addition of the three-item scale to the traditional model (cancer type, stage, age, and KPS) resulted in the net reclassification improvement (NRI) in the discrimination of death events; 26.8% for mortality at 1 year (95% CI; 14.4–38.2, p < 0.001, Table 5) and 29.0% for mortality at 2 years (95% CI; 18.1–37.9, p < 0.001). The calibration plots for the prediction of 1 and 2-year OS are shown in Fig. 2. The calibration plots

Table 3
Prognostic factors for overall survival by univariable analysis.

Variable		HR 95% CI	p value
Patient and cancer-related factors			
	Age; ≥72 vs <72	1.49 (1.12–1.98)	0.007
	Sex; female vs male	0.43 (0.32–0.57)	<0.001
	Physician-rated KPS; ≥80 vs <80	2.33 (1.71–3.17)	<0.001
	Cancer type; breast vs other	0.21 (0.15–0.29)	<0.001
	Stage; 3–4 vs 1–2	4.38 (3.20–6.01)	<0.001
	Treatment intent; curative vs palliative	0.27 (0.20–0.36)	<0.001
Functional status			
MOS-ADL	Vigorous activities; limited vs not limited at all	2.09 (1.27–3.45)	0.004
	Moderate activities; limited vs not limited at all	2.03 (1.53–2.71)	<0.001
	Lifting or carrying groceries; limited vs not limited at all	1.95 (1.47–2.60)	<0.001
	Climbing several flights of stairs; limited vs not limited at all	2.29 (1.68–3.12)	<0.001
	Climbing one flight of stairs; limited vs not limited at all	2.06 (1.54–2.75)	<0.001
	Bending; kneeling; or stooping; limited vs not limited at all	1.42 (1.06–1.90)	0.017
	Walking more than a mile; limited vs not limited at all	2.48 (1.80–3.41)	<0.001
	Walking several blocks; limited vs not limited at all	2.65 (1.98–3.54)	<0.001
	Walking one block; limited vs not limited at all	2.76 (2.06–3.68)	<0.001
	Bathing or dressing yourself; limited vs not limited at all	2.63 (1.83–3.77)	<0.001
IADL	Mobility; requires assistance vs no assistance	2.90 (2.10–4.00)	<0.001
	Shopping; requires assistance vs no assistance	3.13 (2.29–4.28)	<0.001
	Meal preparation; requires assistance vs no assistance	3.28 (2.38–4.52)	<0.001
	Housework; requires assistance vs no assistance	2.27 (1.70–3.03)	<0.001
	Medication intake; requires assistance vs no assistance	2.86 (1.92–4.25)	<0.001
	Handling money; requires assistance vs no assistance	1.89 (1.28–2.80)	0.001
TUG	Timed Up and Go; ≥12 vs <12	2.05 (1.53–2.76)	<0.001
Hearing; eyesight	Hearing; fair/poor/deaf vs excellent/good	1.58 (1.14–2.19)	0.006
	Eyesight; fair/poor/blind vs excellent/good	1.62 (1.15–2.29)	0.006
Nutritional status			
	Unintentional weight loss; ≥5% vs <5%	2.94 (2.18–3.96)	<0.001
Comorbidity			
	No. of comorbid conditions; ≥3 vs <3	1.45 (1.09–1.93)	0.012
Polypharmacy			
	No. of prescribed medication; ≥5 vs <5	1.46 (1.08–1.98)	0.013
Cognition (BOMC)			
	Orientation to time (year); incorrect vs correct	3.69 (1.73–7.88)	0.001
	Count backwards from 20 to 1; incorrect vs correct	2.18 (1.32–3.60)	0.002
	Say the months in reverse order; incorrect vs correct	1.89 (1.32–2.73)	0.001
	Repeat the memory phrase; incorrect vs correct	1.61 (1.20–2.15)	0.001
Psychologic state (MHI-17)			
	Life is full of interesting things; a good bit, most, all vs some, a little, none of the time	0.64 (0.46–0.88)	0.007
	Feeling calm; a good bit, most, all vs some, a little, none of the time	0.66 (0.47–0.93)	0.016
	Feeling moody; a good bit, most, all vs some, a little, none of the time	2.00 (1.18–3.39)	0.010
	Feeling cheerful; a good bit, most, all vs some, a little, none of the time	0.65 (0.48–0.89)	0.007
MOS-social activity			
	Decreased social activity due to health/emotional problems; a little, none vs some, most, all of the time	2.33 (1.73–3.13)	<0.001
	Decreased social activity due to health/emotional problems; somewhat, much less active vs about the same, somewhat, much more active than before	1.90 (1.43–2.54)	<0.001
	Limited social activity compared with others your age, somewhat, much more vs about the same, somewhat, much less limited	2.10 (1.55–2.85)	<0.001
	Health/emotional problems interfered with social activity, moderately, quite a bit, extremely vs not at all, slightly	2.07 (1.53–2.81)	<0.001

Abbreviations: ADL, Activities of Daily Living; BOMC, Blessed Orientation Memory Concentration test; CI, confidence interval; IADL, Instrumental Activities of Daily Living; HR, hazard ratio; MHI-17, Mental Health Inventory-17; KPS, Karnofsky Performance Status; MOS, Medical Outcomes Study; TUG, Timed Up and Go test.

of the three-item scale plus the traditional model revealed better prediction of 1 and 2-year OS compared to the traditional model. These findings indicate that the model including the three-item scale was more accurately able to predict survival than a model relying on the traditional factors.

3.6. Prognostic Value of the Three-item Scale for Incident Cancer Group and Cancer-specific Survival

We performed an exploratory subgroup analysis with 179 patients who completed the GA within 3 months of their date of diagnosis (incident cancer group). The results were similar to those from the entire cohort (Table 6). We also assessed the prognostic value of the three-item scale for cancer-specific survival. In multivariable analysis that included cancer type, stage, age, KPS, and time from diagnosis to complete GA, the three-item scale remained significantly related to cancer-specific survival, as well (Table 6).

3.7. Exploratory Analysis of the Three-item Prognostic Scale

As nearly half of the patients in our study had breast cancer (N = 268), we assessed the prognostic value of the three-item scale in this subgroup. Independent of cancer type, age, KPS and time from diagnosis to GA completion, the three-item scale was a significant predictor of OS.

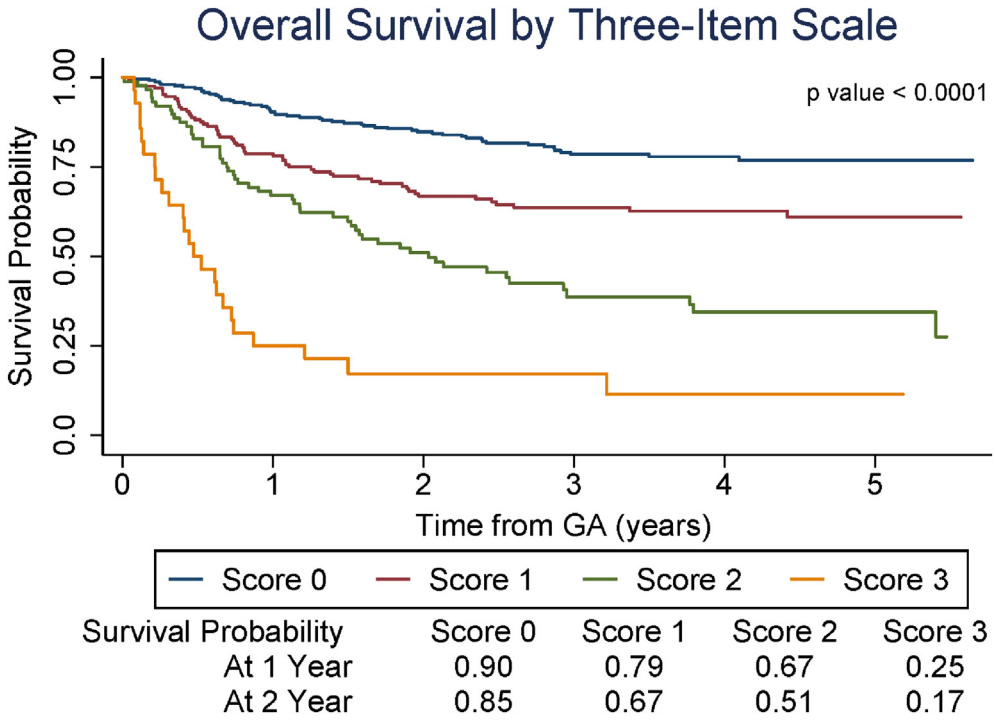

Fig. 1. Kaplan–Meier curve of overall survival using the three-item prognostic scale (N = 546). Score 1 for each of the following three items: "Walking several blocks; limited", "Shopping; requires assistance", and "Unintentional weight loss; ≥5%". Abbreviations: GA, Geriatric Assessment. Range: score 0 = no deficits to score 3 = 3 deficits.

In comparison with score 0, HRs for OS were 2.28 for score 1, 8.78 for score 2, and 12.03 for score 3.

We also performed an exploratory analysis stratified by treatment: curative (N = 407) vs palliative (N = 125) intent treatment groups. The three-item scale was a significant predictor of OS, independent of cancer type, age, KPS and time from diagnosis to GA completion in both groups. In comparison with score 0, HRs for OS were 1.84 for score 1, 3.42 for score 2, and 4.69 for score 3 in curative intent group and HRs for OS were 2.04 for score 1, 2.67 for score 2, and 7.59 for score 3 in palliative intent group.

4. Discussion

In our sample of older outpatients with cancer, we were able to identify 3 items from the GA that were strong significant prognostic factors for overall survival, independent of cancer-related factors, age and performance status. A simple three-item prognostic scale based on these items ("limitation in walking several blocks", "limitation in shopping", and "≥5% unintentional weight loss in 6 months") was able to create prognostic groups with markedly different survival probabilities. Further, the three-item scale improved prognostic discrimination over that of traditional variables alone.

The Karnofsky and ECOG performance status (PS) has been demonstrated to correlate with survival in various cancers [24–26] and most commonly used instruments of functional performance in clinical practice and in research settings [27]. When the three-item scale was included in the traditional prognostic model (cancer type, stage, age and PS), HR for performance status became not significant (HR 1.18, p = 0.44) while HR for the three-item scale remained highly statistically significant (Table 4). This finding suggests that the three-item scale is more sensitive that PS in identifying vulnerabilities that may place older patients at risk of mortality.

The individual components of our three-item scale are markers of impaired physical function and poor nutrition. These have been most consistently reported GA domains associated with OS, including ADL, TUG and Mini-Nutritional Assessment (MNA), correcting for cancer-related factors, despite the fact that the studies are generally heterogeneous in terms of cancer type, stage, treatment and GA tool [4,8,9,28–30]. Recently, Aaldriks et al. evaluated a prognostic value of individual items of the MNA and Groningen frailty indicator (GFI) in a cohort of 494 patients older than 70 years of age with various types of cancer [23]. They identified three prognostic factors for OS using a stepwise selection procedure adjusted for age, sex, cancer type, and purpose of treatment. These factors were "dependence in shopping", "declining food intake in past 3 months" and "using >3 prescription drugs". Their findings are in keeping with our results that function and nutrition items are independent prognostic factors. "Using >3 prescription drugs" was not a significant variable in our univariable survival analysis (HR 1.30, 95% CI; 0.90–1.87, p = 0.17). The median number of prescribed medications was five in our cohort and "Using ≥5 prescription drugs" was a univariable significant variable. However, it was not selected as a significant factor in the stepwise selection procedure. The differences in median number of prescribed medications and/or other variables considered for stepwise selection may have related to our finding that polypharmacy was not an independent prognostic factor for OS.

Table 4
Three-item prognostic scale for overall survival.

For OS analysis (N = 546)	HR	95% CI	p value
Three-item prognostic scale [no. of patients (%)]			
Score 0 [261 (48)]	Ref.		
Score 1 [169 (31)]	1.85	1.25–2.74	0.002
Score 2 [88 (16)]	2.97	1.84–4.78	<0.001
Score 3 [28 (5)]	8.67	4.97–15.15	<0.001
Traditional factors			
Cancer type; breast vs other	0.38	0.25–0.57	<0.001
Stage; 3–4 vs 1–2	2.84	1.92–4.2	<0.001
Age; ≥72 vs <72	1.36	0.99–1.87	0.06
Physician-rated KPS; ≥80 vs <80	1.18	0.77–1.82	0.44
Time from diagnosis to GA completion	0.98	0.91–1.07	0.71

Score 1 for each of the following three items: "Walking several blocks; limited", "Shopping; requires assistance", and "Unintentional weight loss; ≥5%". Abbreviations: CI, confidence interval; GA, Geriatric Assessment; HR, hazard ratio; KPS, Karnofsky Performance Status; OS, overall survival.

Table 5
Incremental prognostic value of the three-item scale beyond the traditional factors.

	C-statistic (95% CI)	NRI (95% CI) for mortality at 1 year	p value	NRI (95% CI) for mortality at 2 year	p value
Traditional factor model	0.76 (0.73–0.79)	Reference		Reference	
Traditional factors + three-item scale model	0.80 (0.77–0.83)	26.8% (14.4–38.2)	<0.001	29.0% (18.1–37.9)	<0.001

Traditional factors include cancer type, stage, age, physician-rated Karnofsky Performance Status, and time from diagnosis to complete GA. Abbreviations: CI, confidence interval; NRI, net reclassification improvement.

There are limitations to this study. First, not all patients completed the GA at their cancer diagnosis. To take this into account, we include a "time from diagnosis to GA completion" variable into the multivariable model as a covariate. We also performed a subgroup analysis to evaluate the three-item scale in patients who completed the GA within 3 months of diagnosis (incident cancer group). The incident cancer group analysis yielded similar results to the entire cohort and similarly categorized the patients into four distinct prognostic groups. Still, a prognostic value of our scale for newly diagnosed patients could not been fully elucidated in this study. However, this limitation of our study is also strength as this scale is predictive of survival at a variety of times in the cancer trajectory. Second, our cohort was heterogeneous, consisting of older adults with various cancer types and stages. While there may be different prognostic factors among patients with specific cancer types and stages, our study identified the common factors that are prognostic of OS in the geriatric oncology population. Third, almost half of the patients had a diagnosis of breast cancer. We performed the exploratory analysis with patients with cancer and showed the three-item scale was a significant predictor of survival in the more homogenous subset of this cohort. The generalizability of our prognostic scale for the broader spectrum of cancer types may be limited. Further evaluation of this model in other cancer populations remains to be done. Fourth, we could not compare our prognostic scale to the existing tools in geriatric oncology [7–10,23] and general geriatrics such as Lee Schonberg Index available in ePrognosis [31–33] because the variables for these tools were not collected in our study. Fifth, detailed treatment information such as intensity and duration was not available. We used the summary treatment variable (curative or palliative intent). The exploratory analysis stratified by the treatment variable showed that the three-item scale was a significant predictor of survival in both groups.

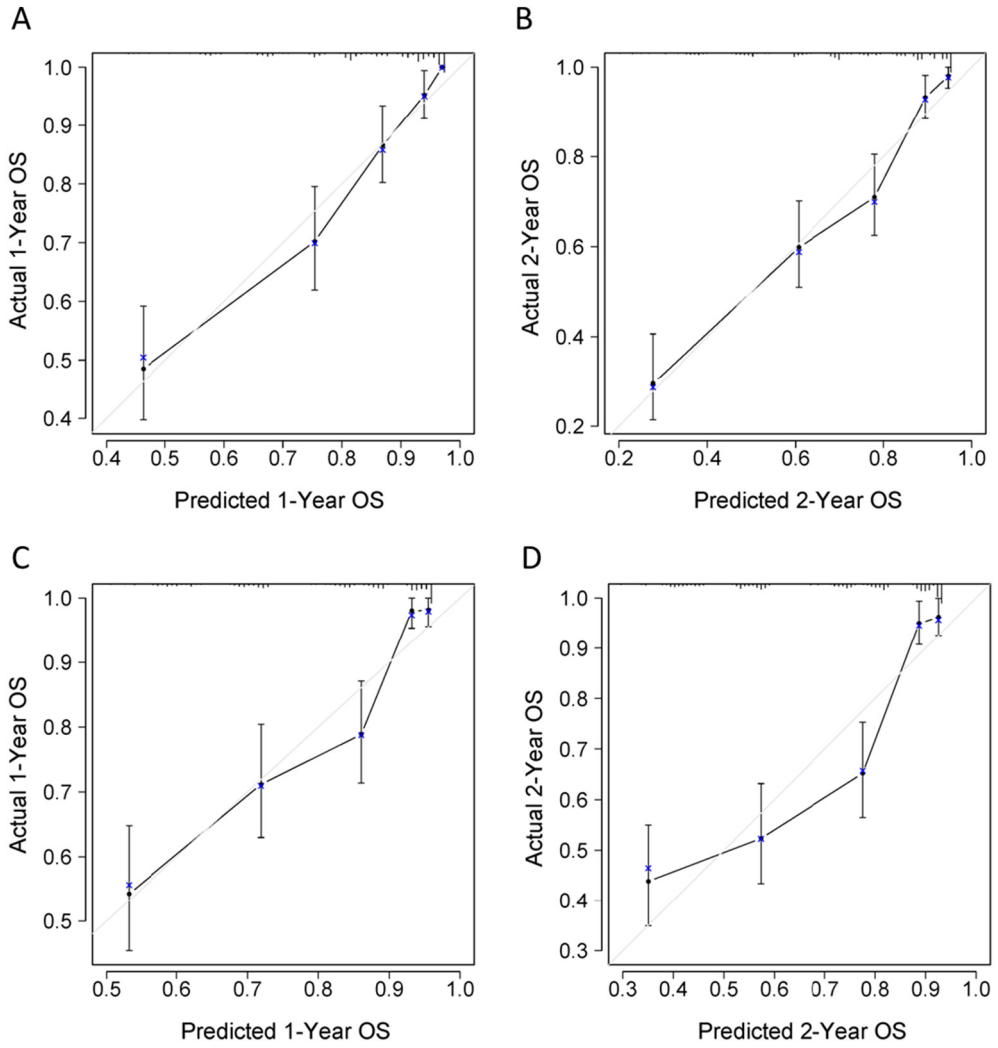

Fig. 2. Calibration plots for 1-year and 2-year overall survival. Traditional factors + three-item scale model: (A) 1-year OS, (B) 2-year OS, traditional factor model: (C) 1-year OS, (D) 2-year OS. Traditional factors include cancer type, stage, age and physician-rated Karnofsky Performance Status, and time from diagnosis to complete GA. Abbreviations: OS, overall survival.

Table 6
Three-item prognostic scale for incident cancer group and cancer-specific survival.

Three-item prognostic scale	No. (%)	HR	95% CI	p value
For OS analysis (incident cancer group, N = 179)				
Score 0	85 (47)	Reference		
Score 1	51 (28)	2.41	1.23–4.72	0.011
Score 2	33 (18)	3.05	1.37–6.77	0.006
Score 3	10 (6)	12.05	4.77–30.46	<0.001
For CSS analysis (N = 546)				
Score 0	261 (48)	Reference		
Score 1	169 (31)	1.74	1.14–2.67	0.011
Score 2	88 (16)	2.44	1.47–4.03	0.001
Score 3	28 (5)	8.18	4.46–14.99	<0.001

Score 1 for each of the following three items: "Walking several blocks; limited", "Shopping; requires assistance", and "Unintentional weight loss; ≥5%". Abbreviations: GA, geriatric assessment. Range: score 0 = no deficits to score 3 = 3 deficits. Models were adjusted for cancer type, stage, age, physician-rated Karnofsky Performance Status, and time from diagnosis to complete GA.
Abbreviations: CI, confidence interval; CSS, cancer-specific survival; HR, hazard ratio; OS, overall survival.

Further evaluation of this model in the setting of treatment remains to be done. Finally, although we conducted an internal model validation, additional external validation studies are warranted.

In conclusion, this study evaluated each items of a cancer-specific GA with respect to association with survival and identified three factors to be prognostic, independent of cancer-related factors, age and performance status. Using these three items which assess function and nutrition, we constructed a three-item prognostic scale which correlated linearly with overall survival and improved on the prognostic accuracy of factors traditionally used in clinical practice. The greatest strength of our prognostic scale is that it is comprised of only three variables that are clinically relevant and easy to obtain even in a busy clinic. If this scale has been externally validated, it can be easily implemented as a useful tool to assess prognosis of older adults with cancer in routine practice. This tool has the potential to help individualize treatment decisions and more accurately stratify older adults for enrollment in cancer clinical trials.

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Disclosures and Conflict of Interest Statements

The authors have no conflict on interests.

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Appendix A. Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2018.01.007.

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