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Research Article

Comparison of Mobility Indices for Predicting Early Death in Older Patients With Cancer: The Physical Frailty in Elderly Cancer Cohort Study

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Abstract

Background: To assess and compare the ability of five mobility indices to predict 6-month mortality in older patients with cancer.

Methods: All consecutive ambulatory older patients with cancer referred for a geriatric assessment before a cancer treatment decision were included in a prospective two-center cohort study (Physical Frailty in Elderly Cancer) between 2013 and 2017. The mobility indices compared were the short physical performance battery, gait speed, hand grip strength, the one-leg stance balance test, and repeated falls. The primary endpoint was 6-month overall mortality. The adjusted hazard ratio (95% confidence interval [CI]) for each mobility index was estimated using a multivariate Cox proportional hazard model adjusted for sex, the Cumulative Illness Rating Scale for Geriatrics, the body mass index, cancer site/extension, and the provision of supportive care alone. The models' predictive performances were assessed in terms of Harrell's C index, net reclassification improvement, and the standardized net benefit.

Results: A total of 603 patients included (mean age: 81.2 ± 6.1 years; women: 54%; metastatic cancer: 45%). In multivariate analyses, an impairment in any of the mobility indices (with the exception of repeated falls) was independently associated with 6-month mortality following a geriatric assessment; the adjusted hazard ratio [95% CI] ranged from 2.35 [1.34–4.13] for the one-leg stance balance (C index: 0.74) to 3.03 [1.93–4.76] for the short physical performance battery (C index: 0.77). For each mobility index, inclusion in the multivariate model improved significantly the latter's prediction of 6-month mortality.

Conclusions: Among mobility tests, short physical performance battery had the best discriminative value for predicting 6-month mortality in older patients with cancer.

Keywords: Mobility limitation, Geriatric assessment, Risk assessment, Neoplasms, Decision support techniques

In western countries, two-thirds of newly diagnosed cancers and three-quarters of cancer-related deaths occur in patients aged 65 or older. Moreover, standardized cancer treatments are difficult to implement in older patients, due to (i) their underrepresentation in cancer trial populations and (ii) their heterogeneity in terms of the

social environment, comorbidities, dependency, nutrition, mobility, mood, and cognitive status. The International Society of Geriatric Oncology (SIOG) recommends the performance of a geriatric assessment (GA) before the cancer treatment decision is taken for older patients; the GA assesses the earlier mentioned heterogeneity and

detects vulnerabilities likely to lead to poor outcomes and treatment complications (1). Mobility (part of the GA) is a well-known predictive factor for mortality in older people (2,3). Furthermore, impaired mobility was found to be independently associated with very short- to long-term mortality in older patients with various cancer sites and stages (4–7).

The SIOG guidelines do not distinguish between mobility and dependency, which are grouped together in the assessment of functional status. Of the 16 tools recommended by the SIOG for the assessment of functional status, 6 are related to mobility: the gait speed (GS), the timed get-up-and-go test, the short physical performance battery (SPPB), the hand grip strength, the one-leg stance balance test, and the number of falls (1).

At present, there is a lack of data on which tool(s) should be recommended for the assessment of mobility in older patients with cancer; the choice of tool depends on (i) the clinician's preferences and habits and (ii) the local availability of geriatric expertise. Hence, there is a need to standardize the tools used in the GA.

On the basis of these considerations, the objective of this study was to assess and compare the ability of five mobility indices to predict 6-month mortality in older patients with cancer.

Methods

Reporting

We followed the STrengthening the Reporting of OBServational studies in Epidemiology guidelines.

Study Design and Population

Patients were recruited from among the members of the Physical Frailty in Elderly Cancer (PF-EC) cohort. The latter prospective, observational two-center cohort study started in November 2013 and is described in detail elsewhere (5). Briefly, all consecutive older in- and outpatients referred for assessment in two geriatric oncology departments (at Avicenne Hospital, Bobigny, France, and Jean Verdier Hospital, Bondy, France) were prospectively included in the PF-EC cohort once (i) a diagnosis of cancer had been established and (ii) frailty was suspected before the cancer treatment decision had been made.

In this study, we analyzed all outpatients, regardless of tumor site, stage or treatment, having joined the cohort before September 30, 2017. We excluded inpatients because walking tests were mostly not measured in this subgroup for practical reasons (eg, infusions limiting walking measurements). The inclusion date was considered to be the date of the patient's first consultation in a participating geriatric oncology department.

All participants provided their informed consent before inclusion in the study. The study was approved by the local investigational review board (Avicenne Hospital, Bobigny, France; reference: CLEA-2015–019).

Cancer-related and Demographic Data

Demographic data (age and sex), cancer-related data (site and extension: local, locally advanced, ie, a non-resectable tumor with no distant metastases, or metastatic), and Eastern Cooperative Oncology Group Performance Status (ECOG-PS) were recorded at the first geriatric oncology consultation, as part of the GA. The type of treatment received by the patient was categorized as either supportive care alone or other care and was recorded during the 6-month follow-up consultation.

Tools Used in the GA

The GA was performed during the patient's first consultation in the geriatric oncology department. Comorbidities were assessed using the Cumulative Illness Rating Scale for Geriatrics (CIRS(G)) (8). Impairment was defined as a total CIRS(G) score above the median of 14, or the presence of at least one grade 3 (severe) comorbidity and/or grade 4 (very severe) comorbidity (apart from the current cancer). Polypharmacy was defined as taking five or more drugs a day (9). Dependency was defined as a six-item activities of daily living (ADL) score less than or equal to 5 of 6, and by a four-item simplified instrumental ADL score (IADL: using the telephone, transport, medications, and money management) of less than 4 of 4 (10,11). Malnutrition was defined as a body mass index (BMI) less than 21 kg/m² (12). Depressed mood was defined as a Mini-Geriatric Depression Scale score of 1 or more of 4 (13). Cognitive impairment was defined as a Mini-Mental State Examination score less than 24 of 30 (14). Finally, impaired mobility was defined as an SPPB score less than 9 of 12.

Vulnerability Screening

The G8 is a vulnerability screening tool for older patients with cancer. It includes eight items: changes in appetite, weight loss, mobility, neurocognitive problems, BMI, the number of medications taken, self-reported health, and age. The total G8 index ranges from 0 to 17, and a score less than or equal to 14 is considered to be abnormal.

Mobility Indices

We studied five mobility indices, all of which were measured during the patient's first consultation in the geriatric oncology department (see details in [Supplementary Material S1](#)).

Gait speed: it was measured with a stopwatch for participants walking over a short distance (4 m, along with a corridor) at their usual pace (2,15,16).

The SPPB: it is a composite walking test that includes measurements of GS (score: 0–4), balance (score: 0–4), and rising from a chair (score 0–4) (17).

Handgrip strength: maximum handgrip strength (in kg) was measured twice for each hand using a hand-held dynamometer (model EH101; Zhongshan Camry Electronic Co., Ltd, Guangdong, China), as a guide to muscle weakness (2).

The one-leg stance balance test: we asked the participant to stand unassisted on one leg for at least 5 seconds. Each leg was tested. An impairment in one-leg stance balance was defined as failure to balance for more than 5 seconds, for one leg or the other (18).

Patient-reported repeated falls: these were defined as at least two falls in the previous year (19).

Furthermore, we classified the five mobility tests as either composite tests (the SPPB) or single-component tests (GS, hand grip strength, one-leg stance balance, and repeated falls).

Outcome

Overall 6-month mortality after the GA was recorded to assess predictors of early death. Vital status was determined by telephoning the patients or their family or by extracting data from medical records.

Statistical Analyses

Descriptive analysis

Categorical variables were summarized as the number (percentage), and continuous variables were summarized as the mean \pm standard

deviation (*SD*) or the median (interquartile range). Baseline characteristics (cancer-related data, demographic data, mobility indices, and other GA components) in the 6-month survivors versus non-survivors were compared in log-rank tests.

Univariate and multivariate analyses

Univariate survival curves were plotted according to the Kaplan–Meier method for the SPPB score, GS, muscle weakness (MW), and the one-leg stance balance test.

We created a basic Cox multivariate proportional hazards regression model to assess factors associated with 6-month mortality. In agreement with recent studies, the model included sex, a total CIRS(G) score above the median of 14, a BMI less than 21 kg/m², the tumor site (reference: breast cancer) and extension (reference: local cancer), and the provision of supportive care alone (4–6,20–25). We checked that these predictors were independently associated with 6-month mortality in our cohort. The model's assumptions were verified. Hazard ratios (HRs) for continuous variables were expressed per *SD*. Each mobility index was included separately in the multivariate model, and its association with the outcome was expressed as an adjusted HR (aHR; 95% confidence interval [CI]). We also estimated the aHR for ECOG-PS and ADL, as these metrics capture (at least in part) the mobility dimension.

The multivariate models' calibration was assessed with the Grönnesby and Borgan goodness-of-fit test. A nonsignificant *p* value (<.05) in a χ^2 test indicated miscalibration.

Discriminant ability of multivariate models

Given the current lack of consensus on the choice of indices for assessing discriminant ability in prediction models (26), we calculated Harrell's C index, the net reclassification improvement (NRI) (27), and the standardized net benefit (SNB) derived from decision curves (28). Harrell's C index is equivalent to the area under the receiver operating characteristic curve for survival data (see details in Supplementary Material S2). Head-to-head comparisons of Harrell's C indices (*p* values) were performed via the *survcomp* package in R.

Owing to the heterogeneity of the early mortality rate in observational studies, we choose three risk thresholds: 10%, 20%, and 30%. To assess the gain in the prediction model's performance by adding a mobility test, we calculated the difference between the SNB (Δ SNB) derived from the multivariate basal prediction model and that derived from a multivariate model implemented with each mobility index. Decision curves were plotted to graphically represent the prediction model's gain in SNB through the addition of a mobility test relative to no risk-assessment.

An initial analysis was performed for the cohort as a whole. We then performed stratified analyses for the metastatic versus nonmetastatic subgroups.

All tests were two-sided, and the threshold for statistical significance was set to *p* value of less than .05. The data were analyzed using R statistical software (version 3.4.3; R Foundation for Statistical Computing, Vienna, Austria; <http://www.r-project.org>). Multivariate imputation by chained equations was used to handle missing data for BMI (*n* = 3), GS (*n* = 3), handgrip strength (*n* = 8), and SPPB (*n* = 2), via the MICE package in R.

Results

Patients

Of the 959 consecutive older (aged 65 and older) patients with cancer in the PF-EC cohort having been referred for a GA up until

September 30, 2017, 356 inpatients were excluded. Hence, 603 outpatients were included in this study.

Baseline Characteristics of Patients, and the 6-Month Mortality Rate

The mean \pm *SD* age of the study population was 81.2 \pm 6.1 years (Table 1). Most of the patients were women (54%) and had solid tumors (94%) and locally advanced (38%) or metastatic cancers (45%). Colorectal and breast cancers were the two most common types. Prostate cancer was uncommon (3%), due to the absence of urological departments in the two participating hospitals. The G8 index was abnormal in 89% patients. The proportion of patients with impaired mobility ranged from 18% to 81.5%, depending on the mobility test and thresholds used. The mortality rate [95% CI] 6 months after the initial GA was 17.9% [14.9–21.2] (*n* = 108/603).

Discriminant Ability of the Unadjusted Mobility Indices

Table 1 also shows univariate associations between each baseline characteristic and 6-month mortality as well as unadjusted HRs for the mobility indices. In univariate analyses, the factors associated with 6-month mortality were as follows: male sex, digestive tract or lung cancers, locally advanced or metastatic cancers, supportive care alone, ECOG-PS more than or equal to 2, G8 index less than or equal to 14, total CIRS(G) score more than 14, number of drugs more than or equal to 5 a day, ADL less than or equal to 5/6 or IADL less than 4/4, BMI less than 21 kg/m², and Mini-Mental State Examination less than 24/30. With the exception of repeated falls, an impaired mobility index (regardless of the tool and thresholds used) was associated with the 6-month mortality rate. The proportion of deceased patients with impaired mobility ranged from 73% to 90%, depending on the index. Figure 1 shows the Kaplan–Meier survival as a function of the baseline SPPB score (<9/12: impaired mobility; \geq 9/12: normal) and baseline GS (<0.8 m/s: impaired mobility; \geq 0.8 m/s: normal). The Kaplan–Meier survival results for handgrip strength were similar to those for GS and are not shown: the 90-day survival rate [95% CI] was 87.5% [83.9–90.3], and the 180-day survival rate was 76.8% [72.3–80.6]. The results for one-leg stance balance are not shown: the 90-day survival rate [95% CI] was 88.2% [84.7–90.8], and the 180-day survival rate was 78.7% [74.5–82.2].

Discriminant Ability of the Mobility Indices Within Multivariate Models

Table 2 shows multivariate associations between each mobility indices and 6-month mortality as well as adjusted HRs. Repeated falls were not considered in the multivariate analyses, due to the absence of an association with mortality in the univariate analysis. In multivariate analyses (adjusted for sex, total CIRS(G) score, BMI, cancer site, cancer extension, and supportive care alone), all the mobility indices (at whatever threshold, except for GS < 1 m/s) were independently associated with 6-month mortality. With continuous variables, the aHR for a decrement of one *SD* of the GS was more than 3, whereas the aHR for a decrement of one *SD* of the other mobility indices was around 1. With clinical thresholds, the aHR for an SPPB score less than 9 of 12 was 3, the aHR for single-component mobility tests (GS, hand grip strength, and one-leg stance balance) ranged from 1.8 to 2.9, and the aHR for the ADL or ECOG-PS was 1.6.

Table 1. Baseline Characteristics of 603 Older Patients With Cancer, and a Comparison of 6-Month Survivors and Nonsurvivors

Variables	Nonsurvivors <i>n</i> = 108 (%)	Survivors <i>n</i> = 495 (%)	Unadjusted hazard ratio [95% CI] for mobility indices	<i>p</i> *
Age, y:				.81
65–74	14 (13)	72 (14.5)		
75–79	27 (25)	114 (23)		
≥ 80	67 (62)	309 (62.5)		
Sex (males)	61 (56.5)	219 (44)		.01
SPPB				
SPPB <9/12	79 (73)	234 (47)	2.89 [1.89–4.43]	<.0001
GS <3/4	63 (58)	185 (37)	2.22 [1.52–3.26]	<.0001
Rising from a chair <3/4	80 (74)	272 (55)	2.30 [1.50–3.54]	.0001
Balance <3/4	52 (48)	179 (36)	1.59 [1.09–2.32]	.01
GS				
Slow GS <1 m/s	97 (90)	395 (80)	2.20 [1.18–4.11]	.01
Slow GS <0.8 m/s	83 (77)	264 (53)	2.73 [1.74–4.27]	<.0001
Slow GS (Fried's phenotype)	71 (66)	214 (43)	2.37 [1.59–3.53]	<.0001
One-leg stance balance test <5 s	93 (86)	356 (72)	2.32 [1.34–4.01]	.002
Handgrip strength				
Muscle weakness (Fried's phenotype)	94 (87)	324 (65)	3.31 [1.89–5.81]	<.0001
Repeated falls (yes)	16 (15)	89 (18)	0.84 [0.49–1.43]	.52
Cancer site				<.0001
Breast	5 (5)	100 (20)		
Colorectal	17 (16)	92 (19)		
Lung	27 (25)	73 (15)		
Prostate	5 (5)	11 (2)		
Liver	12 (11)	73 (15)		
Digestive tract other than colorectal ^a	23 (21)	56 (11)		
Urological malignancies	4 (4)	6 (1)		
Gynecological malignancies	6 (5)	24 (5)		
Hematological malignancies	1 (1)	34 (7)		
Skin and soft tissues	3 (2)	18 (4)		
Others ^b	5 (5)	8 (1)		
Cancer extension				<.0001
Local	8 (7)	96 (19)		
Locally-advanced	30 (28)	198 (40)		
Metastatic	70 (65)	201 (41)		
ECOG-PS ≥2	72 (67)	233 (47)		.0001
G8 index ≤14	103 (95)	432 (87)		.02
Supportive care alone (yes)	37 (34)	87 (17.5)		<.0001
Comorbidities (CIRS(G)):				
Total >14	58 (54)	211 (43)		.03
Number of grade 3 (severe) and/or 4 (very severe)	54 (50)	229 (46)		.42
comorbidities				
Polypharmacy (yes)	83 (77)	319 (64)		.01
Dependency				
ADL ≤5/6	48 (44)	156 (31.5)		.007
IADL <4	79 (73)	307 (62)		.02
Nutrition				
BMI <21 kg/m ²	24 (22)	59 (12)		.003
Mood				
Mini-GDS ≥1/4	55 (51)	206 (42)		.07
Cognition				.009
MMSE ≥24/30	25 (23)	187 (38)		
MMSE <24/30	46 (47)	170 (34)		
Not available	37 (34)	138 (28)		

Note: ADL: activities of daily living; BMI: body mass index; CIRS(G): Cumulative Illness Rating Scale for Geriatrics; ECOG-PS: Eastern Cooperative Oncology Group performance status; GS: gait speed; IADL: instrumental activities of daily living; Mini-GDS: Mini-Geriatric Depression Scale; MMSE: Mini-Mental State Examination; SPPB: short physical performance battery.

^aEsophagus (*n* = 9), gastric (*n* = 20), pancreas (*n* = 28), bile ducts (*n* = 15), anal (*n* = 3), gastrointestinal stoma tumor (*n* = 4).

^bUnknown primary site (*n* = 10), head and neck (*n* = 3); Mobility tests are indicated in bold type.

*Log rank test.

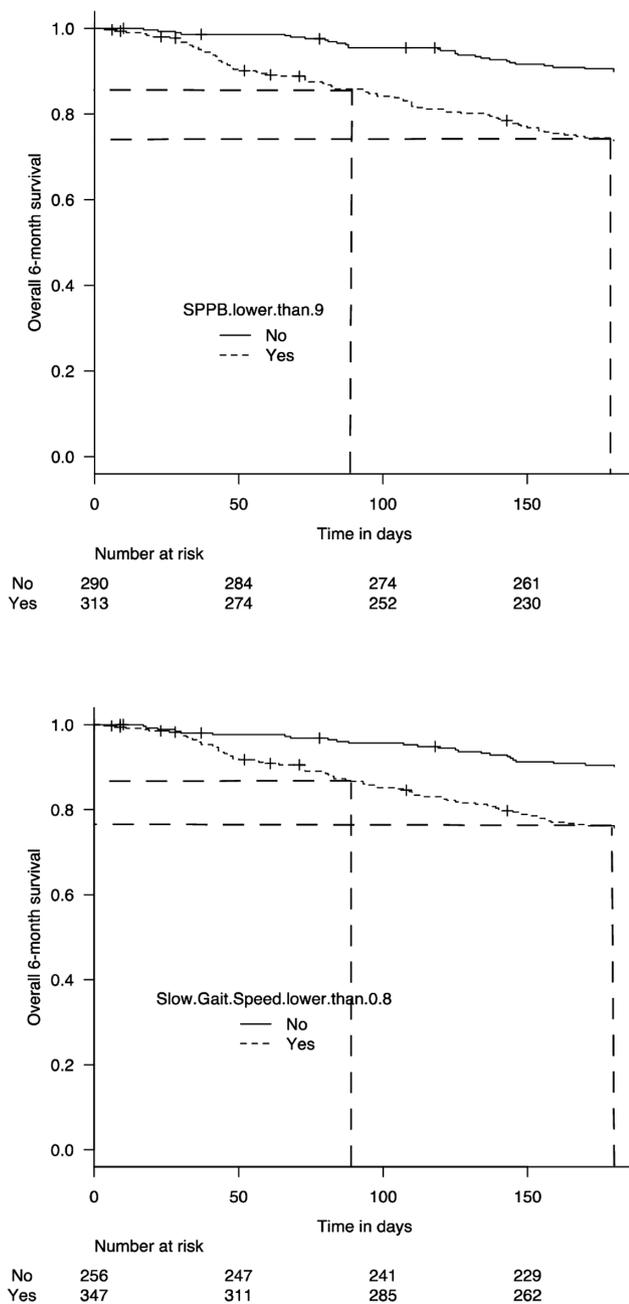


Figure 1. Six-month Kaplan–Meier survival as a function of mobility test impairments in 603 older patients with cancer. Short Physical Performance Battery (SPPB, 0–12): survival rate (%) 90-day: 85.1 (80.6–88.7); 180-day: 73.8 (68.4–78.4). Gait speed (GS, m/s): Survival rate (%) 90-day: 86.1 (81.9–89.4); 180-day: 75.3 (70.3–79.5). 209 × 297 mm (300 × 300 DPI).

Comparison of Mobility Indices for Predicting 6-Month Mortality

Table 2 also provides a comparison of the discriminant ability of multivariate models for the study population as a whole. The discriminant ability (measured as Harrell’s C index) of the basal multivariate model (ie, adjusted for sex, the total CIRS(G) score, the BMI, the cancer site, the cancer extension, and supportive care alone) was 0.72. All the models were well calibrated. The addition of mobility indices to the basal multivariate model increased significantly Harrell’s C index (0.74 to 0.77 depending of mobility indices).

Multivariate model including SPPB was significantly more discriminant than multivariate models with other mobility indices. With the addition of mobility indices to the basal multivariate model, NRI total ranged from 0 to 0.11. This increase in discriminant power mainly concerned NRI, which ranged from 0.01 to 0.09 (data not shown). Regardless of the risk threshold chosen (ie, 10%, 20%, or 30%), the addition of a mobility index increases the difference in the SNB between the basal model and additive models (from 1% to 12%). Figure 2 summarizes the incremental values (according to the decision-curves) of the SPPB score and GS for models predicting 6-month mortality in the whole-study cohort. The results for hand-grip strength and one-leg stance balance were similar to those for GS and are not shown.

Analyses stratified by the cancer stage showed consistent results for the study population as a whole (see Supplementary Table 3). Rising from a chair less than 3/4 was not independently associated with early death in nonmetastatic subgroup, whereas balance test less than 3/4 was not independently associated with early death in the metastatic subgroup. The addition of a mobility index consistently improved discriminant ability, whatever the subgroup.

In absolute terms (according to Harrell’s C index, NRI, and SNB), models that included the composite mobility test (the SPPB) had a consistently better discriminant ability than models that included a single-component mobility test.

Discussion

With the exception of repeated falls, all the mobility tests assessed here (the SPPB, GS, hand grip strength, and the one-leg stance balance test) were independently associated with 6-month mortality in ambulatory older patients with cancer at various sites and stages. The use of mobility test data improved significantly the predictive performance of models of 6-month mortality. Overall, the best test was the SPPB in terms of predictive value and discriminant ability.

Our results are consistent with a recent study (29) and can be explained by the fact that impaired mobility reflects sarcopenia and frailty—both of which are closely linked to pathological aging. Sarcopenia is defined as the age-associated loss of skeletal muscle mass, which in turn leads to the loss of muscle strength and/or poor physical performance. Furthermore, sarcopenia is highly prevalent in cancer (30). Frailty corresponds to abnormally high vulnerability to stressors; a reduced ability to maintain or regain homeostasis after a destabilizing event leads to poor outcomes (early death, disability, unplanned hospitalization, and falls) (15). Hence, a sarcopenia-centered pathway leads to a frailty phenotype, of which impaired mobility represents the first clinically visible sign (2). The SPPB’s good predictive performance might be due to its multidimensional ability to capture mobility (gait, balance, and muscle strength), sarcopenia (gait and muscle strength), and frailty (gait and muscle strength).

The ECOG-PS or ADL metrics are also good predictors of survival. These are the tools most frequently used by oncologists (ECOG-PS) and geriatricians (ADL) to assess a patient’s functional status. Our present results suggest that mobility measures are better predictors of early death than the ECOG-PS and ADL are. This might be due to the fact that the ECOG-PS and ADL are less objective metrics than mobility tools. Moreover, a mobility impairment precedes dependency (ie, an ADL or ECOG-PS impairment) in older people, and it may represent an early marker of frailty and its consequences (early death, dependency, falls, and unplanned hospitalization) (15,31).

Our study had several strengths. First, its prospective design featured the consecutive inclusion of patients and the analysis of five

Table 2. Predictive Ability of Mobility Indices for 6-Month Mortality in 603 Older Patients with Cancer

Models	Adjusted hazard ratio		Calibration		Discriminant ability		NRI total [lower-upper]	ΔSNB (%) at a risk threshold of 20% for early death	
	[95% CI]	1 (Reference)	Goodness of fit (Grönnesby and Borgan test)	Harrell's C index		p ^a			p ^b
				[95% CI]	Reference				
Basal ^c		1 (Reference)	0.13	Reference		Reference	—	—	
Basal + continuous variables									
SPPB per 4 points of less	1.13 [1.07-1.18]		0.73	<.0001	0.72 [0.67-0.78]	Reference	0.09 [-0.01 to 0.28]	8.1	
Gait speed (SPPB) per 1 point of less	1.38 [1.23-1.52]		0.71	.0002	0.76 [0.71-0.82]	—	0.11 [-0.01 to 0.25]	9.9	
Rising from a chair (SPPB) per 2 points of less	1.33 [1.18-1.47]		0.55	.001	0.75 [0.70-0.81]	—	0.05 [-0.04 to 0.24]	7.2	
Balance (SPPB) per 1 point of less	1.26 [1.12-1.39]		0.21	.0004	0.75 [0.69-0.80]	—	0.04 [-0.02 to 0.18]	5.5	
Gait speed per 0.4 m/s of less	3.37 [2.82-3.91]		0.08	.0008	0.76 [0.70-0.81]	.01	0.08 [-0.02 to 0.23]	7.9	
Grip strength per 8 kg of less	1.07 [1.03-1.10]		0.44	.003	0.74 [0.69-0.79]	.06	0.02 [-0.02 to 0.22]	9.0	
ECOG-PS per 1 point of more	1.33 [1.15-1.50]		0.07	.009	0.74 [0.69-0.80]	.004	0.06 [-0.03 to 0.19]	6.2	
ADL per 1 point of less	1.29 [1.15-1.42]		0.71	.004	0.74 [0.69-0.80]	.004	0.06 [-0.03 to 0.15]	6.9	
Basal + clinical thresholds									
SPPB <9/12	3.03 [1.93-4.76]		0.16	<.0001	0.77 [0.71-0.82]	Reference	0.08 [-0.02 to 0.30]	11.8	
Gait speed (SPPB) <3/4	2.34 [1.54-3.56]		0.11	.001	0.75 [0.70-0.81]	—	0.07 [-0.03 to 0.21]	7.6	
Rising from a chair (SPPB) <3/4	2.09 [1.32-3.30]		0.21	.002	0.75 [0.69-0.80]	—	0 [-0.05 to 0.17]	5.3	
Balance (SPPB) <3/4	1.82 [1.21-2.72]		0.54	.002	0.74 [0.69-0.80]	—	0 [-0.05 to 0.17]	7.6	
Gait speed <1 m/s	1.75 [0.92-3.35]		—	—	—	—	—	—	
Gait speed <0.8 m/s	2.59 [1.61-4.17]		0.16	.001	0.75 [0.70-0.81]	.02	0.09 [-0.01 to 0.26]	6.7	
Gait speed (Fried's phenotype)	2.35 [1.53-3.59]		0.70	.001	0.75 [0.70-0.81]	.006	0.08 [-0.04 to 0.23]	6.0	
One-leg stance balance <5 s	2.35 [1.34-4.13]		0.75	.02	0.74 [0.69-0.79]	.002	0.02 [-0.05 to 0.16]	5.1	
Muscle weakness (Fried's phenotype)	2.90 [1.63-5.16]		0.25	.007	0.75 [0.69-0.80]	.04	0.08 [-0.04 to 0.24]	7.2	
ECOG-PS ≥ 2	1.63 [1.07-2.47]		0.50	.05	0.73 [0.68-0.79]	.0001	0 [-0.05 to 0.15]	5.1	
ADL ≤ 5	1.68 [1.12-2.51]		0.15	.05	0.73 [0.69-0.79]	.0001	0.01 [-0.05 to 0.16]	5.5	

Note: NRI = net reclassification improvement; ΔSNB = standardized net benefit difference between full model and the basal model; ADL = activities of daily living; ECOG-PS = Eastern Cooperative Oncology Group performance status; SPPB = short physical performance battery.

^ap Value for comparison of Harrell's C index between basal model and each model with mobility indices.

^bp Value for comparison of Harrell's C index between SPPB and each other mobility indices; ^cSex + Total CIRS(G) score + BMI + Cancer site + Cancer extension + Supportive care only; Continuous variables were shown per their standard deviations.

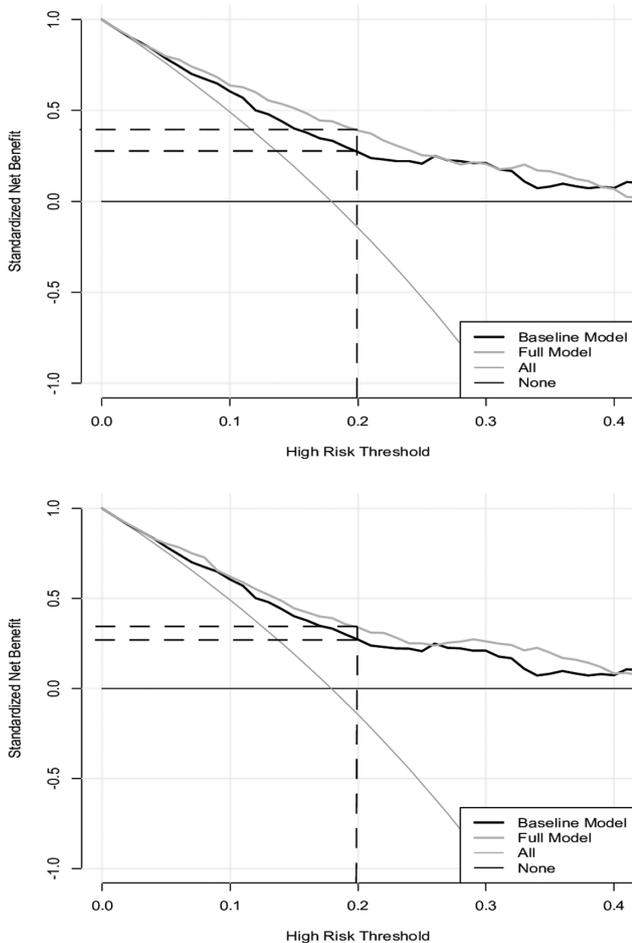


Figure 2. Gain of prediction (%) of 6-month mortality in the whole cohort of older patients with cancer ($n = 603$) by adding a mobility test to the basal prediction model. Cross-line (in gray): assuming that all patients will dead during the 6-month follow-up; Baseline: assuming that no patients will dead during the 6-month follow-up; Curves: the prediction models (the basal prediction model in black, and the full prediction model with a mobility test in gray). At a given risk threshold for early death, the graphs give the expected standardized net benefit (SNB) per patient relative to no risk assessment for adding a mobility test to the basal prediction model for 6-month mortality (adjusted for sex, CIRS(G) score, body mass index [BMI], cancer site/extension and supportive care alone) in ambulatory older patients with cancer, following a geriatric assessment (GA). Short physical performance battery (SPPB) $<9/12$: eg, at a risk threshold of 20% for early death, the addition of the SPPB score to the basal prediction model increased the SNB by 11.8%. Slow gait speed (GS) <0.8 m/s: eg, at a risk threshold of 20% for early death, the addition of GS to the basal prediction model increased the SNB by 6.7%.

different mobility indices. Second, the characteristics of the study population (age, cancer site, and extension at inclusion) were similar to those in other large studies of older patients with cancer (eg. ELCAPA and ONCODAGE). Third, the present results are robust because we used three different indices to assess the models' predictive ability (Harrell's C index, NRI, and SNB).

The study also had limitations—notably the absence of the timed get-up-and-go test, one of the most frequently used mobility tests in GAs of older patients with cancer (1). Given that timed get-up-and-go test is a composite mobility test that assesses gait and lower-limb strength, we believe that it would have had much the same predictive ability as the SPPB did here. Moreover, as SNB is a novel metric for

assessing clinical utility, there are challenges in using and interpreting it appropriately (32). The choice of the risk threshold is one of the challenges. Further studies are needed to validate our findings.

Our present results confirmed the importance of using mobility tests in general (as emphasized in the SIOG guidelines) and the SPPB in particular and highlighted the need to assess mobility during a GA in older patients with cancer. We strongly recommend (i) the incorporation of mobility indices in outcome prediction models and (ii) the use of mobility indices in the treatment decision-making process in geriatric oncology; mobility indices probably capture the frailty dimension earlier than ADL or ECOG-PS do.

Conclusions

In a study of ambulatory older patients with cancer at various sites and stages, all mobility test results (with the exception of repeated falls) were independently associated with 6-month mortality and improved the performance of prediction models. The SPPB was the best in terms of predictive value and discriminant ability.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflicts of Interest

None reported.

References

- Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol*. 2014;32:2595–2603. doi:10.1200/JCO.2013.54.8347
- Fried LP, Tangen CM, Walston J, et al.; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146–M156.
- Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA*. 2011;305:50–58. doi:10.1001/jama.2010.1923
- Soubeyran P, Fonck M, Blanc-Bisson C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. *J Clin Oncol*. 2012;30:1829–1834. doi:10.1200/JCO.2011.35.7442
- Pamoukdjian F, Lévy V, Sebbane G, et al. Slow gait speed is an independent predictor of early death in older cancer outpatients: results from a prospective cohort study. *J Nutr Health Aging*. 2017;21:202–206. doi:10.1007/s12603-016-0734-x
- Ferrat E, Paillaud E, Laurent M, et al.; ELPACA Study Group. Predictors of 1-year mortality in a prospective cohort of elderly patients with cancer. *J Gerontol A Biol Sci Med Sci*. 2015;70:1148–1155. doi:10.1093/geronol/glv025
- Cesari M, Cerullo F, Zamboni V, et al. Functional status and mortality in older women with gynecological cancer. *J Gerontol A Biol Sci Med Sci*. 2013;68:1129–1133. doi:10.1093/geronol/glt073
- Miller MD, Paradis CF, Houck PR, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. *Psychiatry Res*. 1992;41:237–248.

9. Gnjdjic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol*. 2012;65:989–995. doi:10.1016/j.jclinepi.2012.02.018
10. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist*. 1970;10:20–30.
11. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9:179–186.
12. Raynaud-Simon A, Revel-Delhom C, Hébuterne X; French Nutrition and Health Program, French Health High Authority. Clinical practice guidelines from the French Health High Authority: nutritional support strategy in protein-energy malnutrition in the elderly. *Clin Nutr*. 2011;30:312–319. doi:10.1016/j.clnu.2010.12.003
13. Clément JP, Nassif RF, Léger JM, Marchan F. [Development and contribution to the validation of a brief French version of the Yesavage Geriatric Depression Scale]. *Encephale*. 1997;23:91–99.
14. 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;12:189–198. doi:10.1016/0022-3956(75)90026-6
15. Pamoukdjian F, Paillaud E, Zelek L, et al. Measurement of gait speed in older adults to identify complications associated with frailty: a systematic review. *J Geriatr Oncol*. 2015;6:484–496. doi:10.1016/j.jgo.2015.08.006
16. Pamoukdjian F, Canoui-Poitrine F, Longelin-Lombard C, et al. Diagnostic performance of gait speed, G8 and G8 modified indices to screen for vulnerability in older cancer patients: the prospective PF-EC cohort study. *Oncotarget*. 2017;8:50393–50402. doi:10.18632/oncotarget.17361
17. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol*. 1994;49:M85–M94.
18. Vellas BJ, Wayne SJ, Romero L, Baumgartner RN, Rubenstein LZ, Garry PJ. One-leg balance is an important predictor of injurious falls in older persons. *J Am Geriatr Soc*. 1997;45:735–738.
19. Stel VS, Smit JH, Pluijm SM, Lips P. Balance and mobility performance as treatable risk factors for recurrent falling in older persons. *J Clin Epidemiol*. 2003;56:659–668.
20. Bairey O, Bar-Natan M, Shpilberg O. Early death in patients diagnosed with non-Hodgkin’s lymphoma. *Ann Hematol*. 2013;92:345–350. doi:10.1007/s00277-012-1623-y
21. Boulahssass R, Gonfrier S, Ferrero J-M, et al. Predicting early death in older adults with cancer. *Eur J Cancer Oxf Engl*. 1990. 2018;100:65–74. doi:10.1016/j.ejca.2018.04.013
22. Grivaux M, Debieuvre D, Herman D, et al. Early mortality in lung cancer: French prospective multicentre observational study. *BMC Pulm Med*. 2016;16:45. doi:10.1186/s12890-016-0205-5
23. Lefur E, Berton-Rigaud D, Boureau AS, Chapelet G, Berrut G, de Decker L. Early death in advanced ovarian cancer in older adults. *J Am Geriatr Soc*. 2014;62:976–977. doi:10.1111/jgs.12808
24. Vaz-Luis I, Lin NU, Keating NL, Barry WT, Winer EP, Freedman RA. Factors associated with early mortality among patients with de novo metastatic breast cancer: a population-based study. *Oncologist*. 2017;22(4):386. doi:10.1634/theoncologist.2016-0369
25. Zhao H, Zhao Y, Zhang Y, et al. Difference in causes and prognostic factors of early death between cohorts with de novo and relapsed acute promyelocytic leukemia. *Ann Hematol*. 2018;97(3):409–416. doi:10.1007/s00277-017-3216-2
26. Pepe MS, Fan J, Feng Z, Gerds T, Hilden J. The Net Reclassification Index (NRI): a misleading measure of prediction improvement even with independent test data sets. *Stat Biosci*. 2015;7:282–295. doi:10.1007/s12561-014-9118-0
27. Pencina MJ, D’Agostino RB, Vasan RS. Statistical methods for assessment of added usefulness of new biomarkers. *Clin Chem Lab Med*. 2010;48:1703–1711. doi:10.1515/CCLM.2010.340
28. Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. *Med Decis Making*. 2006;26:565–574. doi:10.1177/0272989X06295361
29. Veronese N, Stubbs B, Fontana L, et al. A comparison of objective physical performance tests and future mortality in the elderly people. *J Gerontol A Biol Sci Med Sci*. 2017;72:362–368. doi:10.1093/gerona/glw139
30. Pamoukdjian F, Bouillet T, Lévy V, Soussan M, Zelek L, Paillaud E. Prevalence and predictive value of pre-therapeutic sarcopenia in cancer patients: a systematic review. *Clin Nutr*. 2018;37:1101–1113. doi:10.1016/j.clnu.2017.07.010
31. Perera S, Patel KV, Rosano C, et al. Gait speed predicts incident disability: a pooled analysis. *J Gerontol A Biol Sci Med Sci*. 2016;71:63–71. doi:10.1093/gerona/glv126
32. Kerr KF, Brown MD, Zhu K, Janes H. Assessing the clinical impact of risk prediction models with decision curves: guidance for correct interpretation and appropriate use. *J Clin Oncol*. 2016;34:2534–2540. doi:10.1200/JCO.2015.65.5654