

Research Article

A Comparison of Objective Physical Performance Tests and Future Mortality in the Elderly People

Nicola Veronese,^{1,*} Brendon Stubbs,^{2,3,*} Luigi Fontana,^{4,5,6,*} Caterina Trevisan,¹ Francesco Bolzetta,¹ Marina De Rui,¹ Leonardo Sartori,⁷ Estella Musacchio,⁷ Sabina Zambon,^{5,8} Stefania Maggi,⁸ Egle Perissinotto,⁹ Maria Chiara Corti,¹⁰ Gaetano Crepaldi,⁸ Enzo Manzato,^{1,8} and Giuseppe Sergi¹

¹Geriatrics Division, Department of Medicine–DIMED, University of Padova, Italy. ²Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, UK. ³Health Service and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience King's College London, London, UK. ⁴Department of Clinical and Experimental Sciences, Brescia University, Italy. ⁵Department of Medicine, Washington University School of Medicine, St Louis, Missouri. ⁶CEINGE Biotechnologie Avanzate, Napoli, Italy. ⁷Department of Medicine–DIMED, ClinicaMedica I, University of Padova, Italy. ⁸National Research Council, Neuroscience Institute, Padova, Italy. ⁹Biostatistics, Epidemiology and Public Health Unit, Department of Cardiac, Thoracic and Vascular Sciences, University of Padova, Padova, Italy. ¹⁰Division of Health Care Planning and Evaluation of the Regione Veneto, Venice, Italy.

*These authors contributed equally to this work.

Address correspondence to Nicola Veronese, MD, Geriatrics Division, Department of Medicine–DIMED, University of Padova, Via Giustiniani, 2, 35128 Padova, Italy. E-mail: ilmannato@gmail.com

Received January 25, 2016; Accepted July 6, 2016

Decision Editor: Stephen Kritchevsky, PhD

Abstract

Background: Physical performance is an important predictor of mortality, but little is known on the comparative prognostic utility of different objective physical performance tests in community-dwelling older adults. We compared the prognostic usefulness of several objective physical performance tests on mortality, adjusting our analyses for potential confounders.

Methods: Among 3,099 older community-dwelling participants included in the Progetto Veneto Anziani study, 2,096 were followed for a mean of 4.4 years. Physical performance tests measured were Short Physical Performance Battery (SPPB), 4-meter gait speed, chair stands time, leg extension and flexion, handgrip strength, and 6-Minute Walking Test (6MWT), treated as continuous variables and categorized in gender-specific quartiles. The main outcome was mortality assessed with death certificates.

Results: Participants who died during the follow-up ($n = 327$) scored significantly worse in all physical performance tests measured at baseline than those who survived ($n = 1,769$). Using a Harrell's C-index, the highest C-index was observed for 6MWT in men (C-index = 0.735; 95% confidence interval [CI]: 0.701–0.770, $p < .0001$) and SPPB in women (C-index = 0.781; 95% CI: 0.740–0.822, $p = .0009$). However, in both genders, only SPPB, 4-meter walking speed, and 6MWT are significant predictors of mortality. Analyses using sex-specific quartiles substantially confirmed these findings.

Conclusions: Slow gait speed, 6MWT, and SPPB are significant predictors for mortality in community-dwelling older men and women. Physicians should consider using these tests to identify elderly individuals who are at higher risk of death to improve clinical decision making.

Keywords: Mortality—Physical activity—Physical performance

Physical performance is an important determinant of successful ageing, and if affected, can negatively influence the individual's capability, defined as the ability to undertake the physical tasks of

everyday living (1). In recent years, it has been shown that poor physical performance can predict future risk of fractures, disability, and possibly cardiovascular disease (CVD), especially in older

adults (2,3). However, little is known about the predictive role of objective physical performance tests on mortality risk in elderly men and women.

Data from a meta-analysis involving nine large cohort studies demonstrated that slower gait speed is associated with an increased risk of future mortality (4). This finding was confirmed in a subsequent study, which found good evidence that reduced handgrip strength, slow gait speed, and chair stand are predictors of future mortality (5). Nonetheless, the studies published to date have suffered from several methodological limitations. In particular, small sample size, inadequate sex representation, short duration of follow-up, appropriate adjustment for multiple and relevant confounding factors, and a lack of comparative data considering simultaneous testing of several objective physical performance measures in men and women (6–11).

Given all of the aforementioned, we set out to compare the prognostic usefulness of several objective and well-known physical performance tests (SPPB and its items, handgrip strength, lower limb muscle strength, and 6-Minute Walking Test [6MWT]) on mortality in a large representative cohort study of community-dwelling older adults over 4.4 years while adjusting for multiple pertinent confounders. We also investigated whether sex-specific differences were evident on mortality outcomes. We hypothesized that all physical performance measures would predict mortality.

Methods

Data Source and Subjects

The data included participants from the *Progetto Veneto Anziani* (Pro.V.A.), an observational cohort study among Italian adults aged 65 years and older. The study population initially included 3,099 age- and sex-stratified Caucasian participants (1,854 women and 1,245 men) randomly selected between 1995 and 1997 using a multistage stratification method. Sampling procedures and data collection methods have been extensively described elsewhere (12). One follow-up was made after 4.4 ± 1.2 years from baseline evaluation. The ethical committees of Padova University and the Local Health Units (USSL) n. 15 and n. 18 of the Veneto Region approved the study protocol, and participants gave their written informed consent.

Clinical Data

Participants were examined at city hospitals by trained physicians and nurses. Information was collected during a face-to-face interview. Regular physical activity was defined as ≥ 4 hour/week in the previous month of at least moderate physical activity (eg, brisk walking, cycling, gardening, dancing, or physical exercising), being 4 hour/week the median value of the PRO.V.A. sample. Monthly income was categorized as ≥ 500 versus < 500 €, being 500 € the median value of the sample as whole. Smoking status was classified as “current” versus “never”/“previous” (for at least 1 year in the past). Alcohol drinking was categorized as “yes” versus “no” in the previous month. Educational level was categorized as ≥ 5 versus < 5 years of schooling (which corresponds to the years of primary education in Italy). Functional status was assessed using the Katz’s activities of daily living score. Any depressive symptoms were assessed with the Geriatric Depression Scale (GDS), a 30-item self-reporting tool for identifying depression that has been validated for use in the elderly people (13). Cognitive status was evaluated through 30-items Mini-Mental State Examination (MMSE) score (14). MMSE was not available for five participants.

Nutritional status was evaluated through body mass index and the Geriatric Nutrition Risk Index (GNRI), an index combining albumin levels and actual weight compared with ideal body weight (Wlo) and calculated as follows: $GNRI = [(albumin \times 1.489) + (41.7 \times measured\ weight/Wlo)]$ (15). Data about GNRI/body mass index was missing in three participants.

The presence of diabetes, CVD, hypertension, orthostatic hypotension, osteoarthritis, fractures, chronic obstructive pulmonary disease, or cancer was ascertained by board-certified physicians involved in the study, who examined all of the clinical information collected for each participant. Additional information included disease history, symptoms self-reported using standardized questionnaires, medical and hospital records, blood tests, and a physical examination (12). We considered CVD as the presence of congestive heart failure, angina requiring a stent or angioplasty or hospitalization, myocardial infarction, stroke, atrial fibrillation, or peripheral artery disease. Diabetes was defined as fasting plasma glucose levels ≥ 7.0 mmol/L, glycosylated hemoglobin (HbA1c) $\geq 6.5\%$, the use of glucose-lowering drugs, or a history of a 2-hour postload glucose ≥ 11.1 mmol/L (16). Hypertension was defined as the presence of measured systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or current use of antihypertensive medications (17). Orthostatic hypotension was defined as a drop of at least 20 mmHg in systolic or at least 10 mmHg in diastolic blood pressure in one of the two measurements (18). Renal function was evaluated using the Modification of Diet in Renal Disease (MDRD) study equation that was not recorded in three participants.

Objective Physical Performance Measures

Physical performance and muscle strength measures were assessed using standardized objective performance tests that have previously been used extensively in the literature. Since a significant difference existed between genders for all the parameters investigated ($p < .001$), the quartiles were calculated using gender-specific cutoffs for each test.

- SPPB (6) scores were derived from three objective physical function tests. Each test scored from 0 (inability to complete the test) to 4 (highest level of performance). The scores for all three tests were pooled to obtain a composite score of 0 to 12, higher scores reflecting a better physical function. The cutoffs for dividing the sample into quartiles were 9, 11, and 11 points in men and 8, 9, and 11 points in women.
 - ✓ *Tandem test*: participants were asked to maintain their balance in side-by-side, semi-tandem, and full-tandem positions.
 - ✓ *4-m Walking speed*: the best performance achieved in two walks at participants’ usual pace along a 4-meter corridor was recorded in meters per second. Participants were allowed to use canes or walkers.
 - ✓ *Chair stands time*: participants were asked to stand up and sit down five times as quickly as possible, with their hands folded across their chest. The time taken to complete the test, in seconds was recorded.

Since the 4-meter walking speed and chair stands time are predictors of several negative outcomes in older people (19), these parameters were also considered as separate items in this analysis. The cutoffs used for the 4-meter walking speed were 0.71, 0.83, and 0.97 m/s in men and 0.63, 0.74, and 0.85 m/s in women. For the chair stands time, the corresponding cutoffs were 9.3, 10.9, and 13.3 in men and

10.2, 12.1, and 14.7s in women. Participants failing to complete the chair stand test or 4-meter walking speed were inserted in the worst quartile of performance in the analyses.

- *Leg extension and flexion:* knee extensor (quadriceps) and hip flexor (iliopsoas) muscle isokinetic strength was ascertained using a Nicholas Manual dynamometer (BK-7454, Fred Sammons, Inc.). The highest value recorded between the two legs for quadriceps strength was used in this analysis (20). The cutoffs for leg extension were 18, 25, and 34 kg in men and 14, 18, and 24 kg in women; for leg flexion, they were 19, 25, and 31 kg in men and 13, 17, and 22 kg in women.
- *Handgrip strength:* this was measured in kilogram using a JAMAR handheld dynamometer (BK-7498, Fred Sammons, Inc.). The best result obtained at three attempts with each hand was used for our analyses. The cutoffs were 29, 34, and 39 kg in men and 18, 22, and 26 kg in women.
- *6MWT:* participants were asked to walk at their usual pace for 6 minutes, and the distance they covered was recording in meters (21). The cutoffs were 320, 381, and 442 meter in men and 263, 326, and 381 meter in women.

Mortality Surveillance

Survival status was determined at the follow-up evaluation through interviews with the relatives if the participant died. A copy of the official death certificate was obtained. The main cause of death reported in the death certificate was also recorded and classified according to ICD-9 (12).

Statistical Analyses

For the continuous variables, normal distributions were tested using the Shapiro–Wilk test. Participants' characteristics were summarized using means (\pm standard deviations) for continuous variables and counts and percentages for categorical variables, by survival status during follow-up. Age- and gender-adjusted p values were calculated as follows: the differences between the means of the covariates were analyzed for continuous variables using a general linear model; logistic regression was used for categorical variables.

Factors known to be associated with increased mortality in older people were considered for inclusion in the analysis. The predictors included in the final model were all the variables reaching $p \leq .20$ in the univariate analyses assessed with Kaplan–Meier for categorical and Cox's regression analyses for continuous variables, respectively. Multicollinearity among covariates was estimated with the variance inflation factor considering a value ≥ 2 as exclusion criterion. Due to high collinearity with GNRI (variance inflation factor = 5.89), body mass index was excluded. Hazard ratios (HRs) and 95% confidence intervals (CIs) were used to compare survival rates across quartiles of physical performance and muscle strength tests, taking those in the fourth quartile (indicating best scores) for reference. In fully adjusted model, data were missing for 124 (=5.9% of the baseline population).

We investigated the ability of the model to predict risk of mortality using Harrell's C statistic (22), for which the censoring distribution is considered when calculating the concordance probability. We consecutively introduced all the covariates independently associated with mortality in the Cox's regression analysis and, through a step-wise selection, only those with a p -value $< .05$ were kept. Physical performance tests were forced in the models independently from their statistical significance.

Since a significant difference ($p < .001$) existed for the interaction between all exposure and outcome parameters, the analyses were also conducted by gender. In sensitivity analyses, we removed one at the time the factors significantly associated with mortality that could explain gender differences in the association between poor physical performance and survival.

All analyses were performed using the SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois), except Harrell's C -index made with SAS 9.3. All statistical tests were two tailed, and statistical significance was assumed for a p -value $\leq .05$.

Results

Study Flow of Participants

At baseline, from 3,099 eligible older adults, 658 and 345 were excluded due to incomplete physical performance measures and missing mortality data, respectively, leaving 2,096 within the current analyses. Compared with participants included in the current study, those not included were more likely to be men (52.2% vs. 42.0%; $p < .001$) and older (80.6 ± 8.0 vs. 75.2 ± 6.1 ; $p < .001$).

Included Participants Details

The mean age of the 2,096 community-dwelling participants was 75.2 ± 6.1 years [range: 65–103], of which 58.0% were women.

As shown in Table 1, men had a twofold risk of death during follow-up compared with women (23.2 vs. 10.4%, $p < .0001$). Since the interaction between physical performance items at baseline by gender and survival status at follow-up was significant for all the tests included ($p < .05$), the data are stratified according to gender.

A total of 327 participants (=15% of the baseline population) died during the follow-up. Independently from gender, those who died were significantly older than those who survived ($p < .0001$). After adjusting for age, participants who died had lower activities of daily living, MMSE, and GNRI scores (Table 1). Participants who died also had several more comorbidities including CVD and hypertension and used a higher number of medications than those who survived (see Table 1). Deceased men had a significant higher presence of orthostatic hypotension ($p = .02$), whereas deceased women had a higher proportion of chronic obstructive pulmonary disease ($p = .04$) than those alive at follow-up.

Regarding physical performance, deceased men scored significantly worse than those alive in SPPB, gait speed, leg flexion, and 6MWT, whereas women dead at follow-up scored significantly worse in all the items of SPPB, in handgrip and 6MWT (Table 1).

Which Objective Physical Performance Tests Predicted Survival at Follow-up?

Supplementary Table 1 reports the findings of the Harrell's C -index showing that this parameter, when including only covariates significantly associated with mortality, ranges from 0.721 (95% CI: 0.685–0.756) in men to 0.769 (95% CI: 0.727–0.811) in women, respectively. When added singular physical performance items, the highest C -index was observed for 6MWT in men (C -index = 0.735; 95% CI: 0.701–0.770, $p < .0001$) and SPPB in women (C -index = 0.781; 95% CI: 0.740–0.822, $p = .0009$). However, in both genders, only SPPB, 4-meter walking speed and 6MWT are significant predictors of mortality as shown in Supplementary Table 1.

Table 2 reports Cox's regression analyses in the sample as a whole and by gender over a mean follow-up of 4.4 ± 1.2 years. Taking those in the fourth quartile (best physical performance as reference) and

Table 1. Baseline Characteristics of the Study Sample by Survival Status During the Follow-up

Participants' characteristics	Men		Women	
	Deceased (<i>n</i> = 204)	Survived (<i>n</i> = 674)	Deceased (<i>n</i> = 123)	Survived (<i>n</i> = 1,094)
Age (years)	79.1 (7.4)	73.9 (6.9)***	79.2 (7.2)	73.5 (6.4)***
General and anthropometric characteristics				
Alcohol drinking (%)	166 (81.4)	590 (87.5)	72 (41.5)	444 (40.6)
Current smokers (%)	34 (16.7)	114 (16.9)	3 (2.4)	56 (5.1)**
Educational level >5 y (%)	35 (18.2)	141 (21.4)	8 (7.0)	117 (10.9)
Monthly income ≥500 € (%)	101 (50.0)	357 (53.0)	31 (25.8)	301 (28.2)
Physical activity ≥4hr/wk (%)	67 (32.8)	266 (39.5)	16 (13.0)	222 (20.3)
ADL (score)	5.3 (1.2)	5.7 (0.8)	5.1 (1.2)	5.5 (0.9)**
BMI (kg/m ²)	26.2 (3.7)	27.0 (3.7)	27.4 (4.9)	28.1 (4.7)
GDS (score)	8.5 (4.8)	8.1 (3.8)***	10.7 (5.5)	10.3 (5.2)***
MMSE (score)	23.3 (5.1)	25.6 (3.6)***	21.7 (6.1)	24.7 (4.0)***
GNRI (score)	105.4 (5.5)	107.3 (5.1)**	104.9 (5.6)	106.7 (4.9)***
Medical conditions and renal function assessment				
Diabetes (%)	34 (16.7)	102 (15.1)	36 (29.3)	158 (14.4)***
Hypertension (%)	157 (77.3)	463 (68.7)*	101 (82.1)	784 (71.1)
Orthostatic hypotension (%)	73 (36.7)	169 (25.2)*	40 (32.5)	367 (33.8)
CVD (%)	77 (37.7)	149 (22.1)***	36 (29.3)	115 (10.5)***
Osteoarthritis (%)	100 (49.0)	332 (49.3)	94 (76.4)	705 (64.4)
Fractures (%)	14 (6.9)	41 (6.1)	10 (8.1)	93 (8.5)
COPD (%)	46 (22.5)	79 (11.7)**	11 (8.9)	50 (4.6)*
Cancer (%)	31 (15.2)	40 (5.9)***	9 (7.3)	73 (6.7)
eGFR (ml/min)	70.7 (19.1)	75.2 (17.3)	63.1 (18.0)	67.7 (17.6)
Number of medications	3.0 (2.1)	2.2 (2.0)	3.7 (2.3)	2.7 (2.0)**
Physical performance tests				
SPPB (points)	8.7 (2.5)	10.3 (1.8)***	7.3 (2.4)	9.1 (2.1)***
4-m Walking speed (m/s)	0.7 (0.2)	0.9 (0.2)***	0.6 (0.2)	0.8 (0.2)***
Chair stands time (s)	13.3 (5.5)	11.7 (7.8)	16.0 (8.7)	13.4 (7.2)*
Leg extension (kg)	23.8 (14.8)	27.5 (11.7)	17.1 (6.9)	19.7 (10.3)
Leg flexion (kg)	23.0 (13.0)	26.9 (10.9)*	16.5 (6.7)	18.4 (15.4)
Handgrip (kg)	30.7 (8.4)	34.6 (8.1)	18.9 (5.5)	22.1 (5.6)**
6MWT (m)	318.6 (99.4)	393.7 (90.7)***	275.8 (88.8)	326.0 (84.3)***

Notes: Unless otherwise specified, *p* values were adjusted for age using a general linear model or logistic regression, as appropriate. Numbers are means (and standard deviations) or numbers (and percentages) as appropriate. ADL = activities of daily living; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; GDS = Geriatric Depression Scale; GNRI = Geriatric Nutritional Risk Index; MMSE = Mini Mental State Examination.

p* < .05. *p* < .01. ****p* < .001: between survival and deceased by sex.

after adjusting for baseline potential confounders, participants in the two lowest quartiles of SPPB (Q1: HR = 2.06; 95% CI: 1.27–3.34, *p* = .003; Q2: HR = 1.84; 95% CI: 1.10–3.05, *p* = .02; Supplementary Figure 1) carried a significant higher risk of death. Among the items included in SPPB, only slow walking speed was associated with a higher rate of death during the follow-up period (Q1: HR = 1.56; 95% CI: 1.01–2.40, *p* = .04; Supplementary Figure 2), whereas among the other tests investigated only those in the lowest quartile of 6MWT reported a significant higher risk of death (Q1: HR = 2.00; 95% CI: 1.27–3.18, *p* = .003; Supplementary Figure 3).

After stratifying for sex, in men (*n* = 879), the lowest quartile of SPPB, 4-meter walking speed and 6MWT all predicted mortality in the fully adjusted model, whereas none of the physical measures predicted mortality in women (*n* = 1,217; Table 2). In a sensitivity analysis, when we removed GNRI from this model, the HR for the worst quartile of SPPB (HR = 2.11, 95% CI: 1.11–4.57, *p* = .02) and 6MWT (Q1: HR = 1.77, 95% CI: 1.08–3.87, *p* = .03) became significant in women as well. In contrast, the removal of other factors that significantly increased mortality (ie, CVD, diabetes, and current smoking) did not modify the association between these physical performance tests and mortality (data not shown).

Discussion

Although poor physical performance is a well-recognized predictor of mortality in the elderly, a paucity of research studies has considered the comparative prognostic usefulness of multiple physical performance tests. In our study, we compared the prognostic usefulness of seven objective physical performance tests on mortality, adjusting for multiple pertinent confounders, to address limitations in previous studies published on this topic.

At baseline, people that subsequently died scored significantly worse across all measures. The prognostic usefulness of these tests was, however, different since only low SPPB scores, slow gait speed, and 6MWT were significant predictors of mortality in both genders. In women, the prognostic validity of low SPPB and 6MWT scores seems to be influenced by the coexistence of poor nutritional status evaluated through low GNRI. Interestingly, we found no evidence that muscle strength tests or chair stands significantly predict mortality.

Among the physical tests significantly associated with mortality, the prognostic usefulness of SPPB, 4-meter walking speed and 6MWT seems to be similar, independently from gender.

Table 2. Association Between Physical Performance Tests at the Baseline and All-cause Mortality

		Males						Females					
		Number of deaths	Number of people	Unadjusted hazard ratio (95% CI)	p Value	Fully adjusted hazard ratio (95% CI)	p Value	Number of deaths	Number of people	Unadjusted hazard ratio (95% CI)	p Value	Fully adjusted hazard ratio (95% CI)	p Value
SPPB													
Q4	15	194	1 [ref.]	1 [ref.]	.001	1.88 (0.93–3.77)	.08	12	320	1 [ref.]	1 [ref.]	1 [ref.]	.99
Q3	51	268	2.83 (1.54–5.22)	1.88 (0.93–3.77)	.001	1.88 (0.93–3.77)	.08	29	449	1.59 (0.80–3.13)	.18	1.00 (0.50–2.06)	.99
Q2	59	221	4.04 (2.21–7.40)	1.99 (1.06–3.72)	<.001	1.99 (1.06–3.72)	.03	24	157	4.11 (2.05–8.27)	<.001	2.02 (0.93–4.38)	.08
Q1	79	195	6.75 (3.58–11.72)	2.10 (1.10–3.99)	<.001	2.10 (1.10–3.99)	.02	58	292	5.18 (2.76–9.72)	<.001	1.83 (0.85–3.95)	.12
4-m Walking speed													
Q4	21	219	1 [ref.]	1 [ref.]	.04	1.61 (0.94–2.76)	.08	18	320	1 [ref.]	1 [ref.]	1 [ref.]	.93
Q3	45	251	1.73 (1.02–2.93)	1.61 (0.94–2.76)	<.001	1.75 (1.00–3.06)	.05	21	318	1.15 (0.60–2.20)	.66	0.97 (0.50–1.89)	.93
Q2	57	211	2.86 (1.73–4.75)	1.83 (1.08–3.11)	<.001	1.83 (1.08–3.11)	.03	22	268	1.52 (0.80–2.88)	.20	0.84 (0.42–1.67)	.61
Q1	81	197	4.68 (2.88–7.61)	1 [ref.]	<.001	1 [ref.]	.03	62	312	3.58 (2.08–6.18)	<.001	1.64 (0.80–3.35)	.18
Chair stands time													
Q4	25	210	1 [ref.]	1 [ref.]	.01	1.40 (0.84–2.24)	.19	17	286	1 [ref.]	1 [ref.]	1 [ref.]	.57
Q3	50	229	1.91 (1.16–3.15)	1.40 (0.84–2.24)	<.001	1.42 (0.85–2.36)	.18	22	274	1.21 (0.64–2.32)	.56	0.82 (0.42–1.60)	.57
Q2	58	220	2.41 (1.48–3.92)	1.00 (0.59–1.73)	<.001	1.00 (0.59–1.73)	.98	26	281	1.43 (0.77–2.66)	.26	0.94 (0.49–1.80)	.84
Q1	71	219	2.89 (1.78–4.67)	0.73 (0.45–1.19)	<.001	0.73 (0.45–1.19)	.21	58	254	3.22 (1.86–5.57)	<.001	1.66 (0.89–3.09)	.11
Leg extension													
Q4	33	219	1 [ref.]	1 [ref.]	.14	0.81 (0.50–1.32)	.40	23	305	1 [ref.]	1 [ref.]	1 [ref.]	.26
Q3	46	221	1.41 (0.89–2.22)	0.81 (0.50–1.32)	.08	0.90 (0.56–1.44)	.65	24	306	1.00 (0.56–1.79)	.99	0.71 (0.39–1.29)	.26
Q2	56	220	1.50 (0.95–2.37)	0.73 (0.45–1.19)	.001	0.73 (0.45–1.19)	.21	36	303	1.55 (0.91–2.66)	.11	1.16 (0.66–2.03)	.62
Q1	69	218	2.04 (1.32–3.15)	1 [ref.]	<.001	1 [ref.]	.48	40	304	1.44 (0.84–2.49)	.19	0.71 (0.39–1.29)	.26
Leg flexion													
Q4	34	219	1 [ref.]	1 [ref.]	.87	0.66 (0.40–1.10)	.11	23	305	1 [ref.]	1 [ref.]	1 [ref.]	.56
Q3	35	220	0.96 (0.59–1.57)	0.66 (0.40–1.10)	.08	0.77 (0.47–1.24)	.28	30	309	1.27 (0.73–2.21)	.40	1.19 (0.67–2.10)	.56
Q2	53	220	1.49 (0.95–2.33)	1.10 (0.69–1.76)	<.001	1.10 (0.69–1.76)	.68	34	300	1.29 (0.74–2.25)	.36	0.93 (0.53–1.65)	.81
Q1	82	219	2.51 (1.65–3.80)	1 [ref.]	<.001	1 [ref.]	.60	36	304	1.41 (0.82–2.43)	.22	0.80 (0.45–1.43)	.45
Handgrip strength													
Q4	33	227	1 [ref.]	1 [ref.]	.49	0.84 (0.51–1.37)	.48	12	309	1 [ref.]	1 [ref.]	1 [ref.]	.13
Q3	40	227	1.18 (0.74–1.89)	0.84 (0.51–1.37)	.89	0.53 (0.30–1.42)	.47	30	315	2.23 (1.13–4.40)	.02	1.71 (0.86–3.42)	.13
Q2	31	182	1.04 (0.62–1.72)	0.86 (0.49–1.51)	<.001	0.86 (0.49–1.51)	.60	31	322	2.50 (1.29–4.87)	.007	1.16 (0.56–2.37)	.69
Q1	100	242	3.05 (2.03–4.56)	1 [ref.]	<.001	1 [ref.]	.16	50	272	4.30 (2.26–8.17)	<.001	1.27 (0.58–2.75)	.55
6MWT													
Q4	20	222	1 [ref.]	1 [ref.]	.01	1.49 (0.85–2.61)	.16	12	309	1 [ref.]	1 [ref.]	1 [ref.]	.38
Q3	40	218	2.02 (1.17–3.48)	1.32 (0.75–2.30)	.003	1.32 (0.75–2.30)	.33	22	307	1.79 (0.88–3.64)	.11	1.40 (0.66–2.95)	.38
Q2	50	236	2.21 (1.31–3.74)	2.17 (1.21–3.86)	<.001	2.17 (1.21–3.86)	.009	22	301	1.84 (0.91–3.72)	.09	0.85 (0.39–1.85)	.69
Q1	94	202	5.57 (3.47–9.22)	1 [ref.]	<.001	1 [ref.]	.60	67	301	5.52 (2.96–10.30)	<.001	1.81 (0.83–3.90)	.14

Notes: Unless otherwise specified, data are presented as hazard ratios and 95% CIs. CI = confidence interval; SPPB = Short Physical Performance Battery; 6MWT = 6-Minute Walking Test. Significant results in the fully-adjusted models ($p \leq .05$) are highlighted in bold. Q4 indicates those with the best, Q1 those with the worst scores in the physical performance tests. The fully adjusted model included age, preserved activities of daily living, and Mini-Mental State Examination score (all as continuous variables); presence at the baseline of diabetes, hypertension, orthostatic hypotension, cardiovascular diseases, chronic obstructive pulmonary disease, and cancer (all “yes” vs. “no”); renal function; smoking habits (current vs. never/former); geriatric nutritional risk index; and number of medications (both as continuous).

Data from multiple studies have shown that slow walking gait speed is associated with a higher risk of CVD (23), disability (24), repeated hospitalizations (25), and mortality in oncological patients (26). Our data further support the importance of screening community-dwelling older adults for impaired walking gait speed in order to improve clinical and therapeutic decision making. The SPPB test was significantly associated with mortality, it is easy to perform with low time and cost requirements.

A curious finding from our data is that physical performance measures are strong predictors of mortality in males, but in women, the prognostic value of poor physical performance is influenced by their nutritional status when using the categorization in quartiles. This is an important result suggesting that when dealing with elderly women, physicians should monitor not only SPPB scores but also consider the degree of malnutrition. Previous literature has also found that slower gait speed is associated with a slightly increased risk of dressing dependence among women, whereas mobility limitations are approximately the same (24). The exact reasons why malnutrition appears to influence physical performance and the associated mortality risk in women is unclear but might be mediated at least in part by the detrimental impact of malnutrition on sarcopenia in women (27).

In our study, we found that also the 6MWT was associated with mortality reporting also the highest C-index among the tests investigated, but this test can be time consuming in practice and requires space and resources. It has been shown that the 6MWT is associated with higher mortality in patients with chronic obstructive pulmonary disease or other respiratory diseases (28,29), but to the best of our knowledge, there is only one study exploring the possible association between low 6MWT and mortality in community-dwelling older people, finding a no significant association (30). An alternative could be the 400-meter walk test to address the concerns about time and space in the clinical setting.

Poor physical performance levels could be associated to a higher mortality rate through several mechanisms. First, those with poor physical performance usually have higher presence of comorbidities leading to an earlier mortality (like diabetes, CVD, cancer, and chronic obstructive pulmonary disease). However, we attempted to circumvent this limitation by adjusting for these factors in our analyses. Second, low physical performance level is associated also with remarkable endocrine dysfunction, inflammation, and oxidative stress, and all these factors are associated with higher risk of death (5). Finally, low performance physical activity levels seem to be associated to a higher risk of several conditions accelerating the transition to death, including malnutrition, dementia, and CVD (31,32). Thus, poor physical performance might increase the risk of mortality indirectly through the development of such severe comorbidities.

Our findings provide important evidence that physicians should assess physical performance level in older people with objective measures, and not solely rely on self-reported questionnaires, which are characterized by inherent bias and inaccuracy largely due to strong recall bias in older people (33). Consistently, we found no difference in self-reported physical activity level between participants that died and survived at the follow-up, whereas participants who died scored worse across all objective physical performance tests. Poor physical performance might be a potential endophenotype for mortality among this population (5). Interestingly, data from a recent review (34) demonstrated that physical activity plays a key role in the progression of disability, reinforcing the concept that increasing physical activity is one of the most effective preventive strategies in preventing and delaying disability.

This study has a number of limitations and strengths. One potential limitation is the duration of the follow-up. The systematic review and meta-analysis of Cooper and colleagues (5) suggested that for some tests (eg, handgrip strength) it would be better to have a follow-up of 5 years in order to observe an increased risk of mortality. Second, we did not remeasure the changes of physical performance tests assessed at the baseline, and this could affect our findings. Third, due to missing data and loss to follow-up, we encountered a notable dropout among participants. Fourth, the excluded participants and those who dropped out were significantly older males than those included, and this potentially could introduce a bias as well. Finally, no body composition parameters were included in our analyses, and this could play an important role in the association between poor physical performance and mortality.

In conclusion, data from this large longitudinal study indicate that poor physical performance, in particular slow gait speed and SPPB, are risk factors for mortality in older adults. Our data support the importance of routinely screening community-dwelling older adults for impaired walking gait speed with simple and cost-effective tests, such as the SPPB, in order to improve clinical and therapeutic decision making. More studies are needed to understand the effects of physical exercise and nutritional interventions that improve physical performance on mortality risk in community dwelling elderly men and women.

Supplementary Material

Supplementary material can be found at: <http://biomedgerontology.oxfordjournals.org/>

Funding

This work was supported by the data collection phase of the PRO.V.A. study was supported by the Fondazione Cassa di Risparmio di Padova e Rovigo; University of Padova; the Azienda Unità Locale Socio Sanitaria 15 and 18 of the Veneto Region; and a grant from the Veneto Regional Authority (Ricerca Sanitaria Finalizzata n.156/03). The data analysis phase was also financed by a grant from the University of Padova (Population Aging—Economics, Health, Retirement and the Welfare State—POPA_EHR).

Conflict of Interest

The authors have no conflict of interest to declare.

References

1. Kuh D. A life course approach to healthy aging, frailty, and capability. *J Gerontol A Biol Sci Med Sci*. 2007;62:717–721. <http://www.ncbi.nlm.nih.gov/pubmed/17634317>. Accessed November 11, 2015.
2. den Ouden ME, Schuurmans MJ, Arts IE, van der Schouw YT. Physical performance characteristics related to disability in older persons: A systematic review. *Maturitas*. 2011;69:208–219. doi:10.1016/j.maturitas.2011.04.008
3. Reuben DB, Seeman TE, Keeler E, et al. Refining the categorization of physical functional status: The added value of combining self-reported and performance-based measures. *Journals Gerontol Ser A Biol Sci Med Sci*. 2004;59:M1056–M1061. doi:10.1093/gerona/59.10.M1056
4. 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
5. Cooper R, Kuh D, Hardy R. Objectively measured physical capability levels and mortality: Systematic review and meta-analysis. *BMJ*. 2010;341:c4467. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?>

- rtid=2938886&tool=pmcentrez&rendertype=abstract. Accessed July 27, 2015.
6. 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. doi:10.1093/geronj/49.2.M85
 7. Cesari M, Kritchevsky SB, Newman AB, et al. Added value of physical performance measures in predicting adverse health-related events: Results from the Health, Aging and Body Composition Study. *J Am Geriatr Soc.* 2009;57:251–259. doi:10.1111/j.1532-5415.2008.02126.x
 8. Cesari M, Onder G, Zamboni V, et al. Physical function and self-rated health status as predictors of mortality: Results from longitudinal analysis in the iSIRENTE study. *BMC Geriatr.* 2008;8:34. doi:10.1186/1471-2318-8-34.
 9. Cooper R, Kuh D, Cooper C, et al. Objective measures of physical capability and subsequent health: A systematic review. *Age Ageing.* 2011;40:14–23. doi:10.1093/ageing/afq117
 10. Cooper R, Strand BH, Hardy R, Patel KV, Kuh D. Physical capability in mid-life and survival over 13 years of follow-up: British birth cohort study. *BMJ.* 2014;348:g2219. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4004787&tool=pmcentrez&rendertype=abstract>. Accessed November 20, 2015.
 11. Minneci C, Mello AM, Mossello E, et al. Comparative study of four physical performance measures as predictors of death, incident disability, and falls in unselected older persons: The insufficienza Cardiaca negli Anziani Residenti a Dicomano Study. *J Am Geriatr Soc.* 2015;63:136–141. doi:10.1111/jgs.13195
 12. Corti M-C, Guralnik JM, Sartori L, et al. The effect of cardiovascular and osteoarticular diseases on disability in older Italian men and women: Rationale, design, and sample characteristics of the Progetto Veneto Anziani (PRO.V.A.) study. *J Am Geriatr Soc.* 2002;50:1535–1540. <http://www.ncbi.nlm.nih.gov/pubmed/12383151>. Accessed November 3, 2015.
 13. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: A preliminary report. *J Psychiatr Res.* 17:37–49. <http://www.ncbi.nlm.nih.gov/pubmed/7183759>. Accessed August 25, 2014.
 14. Folstein MF, Robins LN, Helzer JE. The Mini-Mental State Examination. *Arch Gen Psychiatry.* 1983;40:812. doi:10.1001/archpsyc.1983.01790060110016
 15. Cereda E, Pedrolli C. The Geriatric Nutritional Risk Index. *Curr Opin Clin Nutr Metab Care.* 2009;12:1–7. doi:10.1097/MCO.0b013e3283186f59
 16. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2005;28(Suppl 1):S37–S42. <http://www.ncbi.nlm.nih.gov/pubmed/15618111>. Accessed August 10, 2015.
 17. Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: Blood pressure measurement in humans: A statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Cou. *Hypertension.* 2005;45:142–161. doi:10.1161/01.HYP.0000150859.47929.8e
 18. American Autonomic Society and the American Academy of Neurology. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. *Neurology.* 1996;46:1470. <http://www.ncbi.nlm.nih.gov/pubmed/8628505>. Accessed September 8, 2015.
 19. Veronese N, Berton L, Carraro S, et al. Effect of oral magnesium supplementation on physical performance in healthy elderly women involved in a weekly exercise program: A randomized controlled trial. *Am J Clin Nutr.* 2014;100:974–981. doi:10.3945/ajcn.113.080168
 20. Bandinelli S, Benvenuti E, Del Lungo I, et al. Measuring muscular strength of the lower limbs by hand-held dynamometer: A standard protocol. *Aging (Milano).* 1999;11:287–293.
 21. Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: A new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J.* 1985;132:919–923. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1345899&tool=pmcentrez&rendertype=abstract>. Accessed November 7, 2015.
 22. Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: Issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med.* 1996;15:361–387. doi:10.1002/(SICI)1097-0258(19960229)15:4<361::AID-SIM168>3.0.CO;2-4
 23. Dumurgier J, Elbaz A, Ducimetière P, Tavernier B, Alperovitch A, Tzourio C. Slow walking speed and cardiovascular death in well functioning older adults: Prospective cohort study. *BMJ.* 2009;339:b4460. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2776130&tool=pmcentrez&rendertype=abstract>. Accessed October 7, 2015.
 24. Perera S, Patel K V, Rosano C, et al. Gait speed predicts incident disability: A pooled analysis. *J Gerontol A Biol Sci Med Sci.* 2015;71:63–71. doi:10.1093/gerona/glv126.
 25. Cawthon PM, Fox KM, Gandra SR, et al. Do muscle mass, muscle density, strength, and physical function similarly influence risk of hospitalization in older adults? *J Am Geriatr Soc.* 2009;57:1411–1419. doi:10.1111/j.1532-5415.2009.02366.x
 26. 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/gerona/glt073
 27. Tay L, Ding YY, Leung BP, et al. Sex-specific differences in risk factors for sarcopenia amongst community-dwelling older adults. *Age (Dordr).* 2015;37:121. doi:10.1007/s11357-015-9860-3
 28. Kempny A, Dimopoulos K, Alonso-Gonzalez R, et al. Six-minute walk test distance and resting oxygen saturations but not functional class predict outcome in adult patients with Eisenmenger syndrome. *Int J Cardiol.* 2013;168:4784–4789. doi:10.1016/j.ijcard.2013.07.227
 29. Durheim MT, Smith PJ, Babyak MA, et al. Six-minute-walk distance and accelerometry predict outcomes in chronic obstructive pulmonary disease independent of Global Initiative for Chronic Obstructive Lung Disease 2011 Group. *Ann Am Thorac Soc.* 2015;12:349–356. doi:10.1513/AnnalsATS.201408-365OC
 30. Mutikainen S, Rantanen T, Alén M, et al. Walking ability and all-cause mortality in older women. *Int J Sports Med.* 2011;32:216–222. doi:10.1055/s-0030-1268506
 31. Barnes DE, Yaffe K, Byers AL, McCormick M, Schaefer C, Whitmer RA. Midlife vs late-life depressive symptoms and risk of dementia: Differential effects for Alzheimer disease and vascular dementia. *Arch Gen Psychiatry.* 2012;69:493–498. doi:10.1001/archgenpsychiatry.2011.1481
 32. Sergi G, Veronese N, Fontana L, et al. Pre-frailty and risk of cardiovascular disease in elderly men and women: The Pro.V.A. study. *J Am Coll Cardiol.* 2015;65:976–983. doi:10.1016/j.jacc.2014.12.040
 33. Schlosser Covell GE, Hoffman-Snyder CR, Wellik KE, et al. Physical activity level and future risk of mild cognitive impairment or dementia: A critically appraised topic. *Neurologist.* 2015;19:89–91. doi:10.1097/NRL.0000000000000013
 34. Tak E, Kuiper R, Chorus A, Hopman-Rock M. Prevention of onset and progression of basic ADL disability by physical activity in community dwelling older adults: A meta-analysis. *Ageing Res Rev.* 2013;12:329–338. doi:10.1016/j.arr.2012.10.001