Relationship Between Renal Function and Physical Performance in Elderly Hospitalized Patients

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Abstract

Chronic kidney disease (CKD) is increasingly recognized as a cause of worsening physical functioning in older patients. The Short Physical Performance Battery (SPPB) is highly reliable in older populations, but no data on older hospitalized patients with different degrees of kidney function are available. We aimed at testing the association between estimated glomerular filtration rate (eGFR) and SPPB, either global score (range 0–12) or its individual components (muscle strength, balance, and walking speed, each ranging from 0 to 4), in a sample of older hospitalized patients. Our series consisted of 486 patients aged 65 or more consecutively enrolled in 11 acute care medical wards participating to a multicenter observational study. eGFR was obtained by the Chronic Kidney Disease Epidemiological Collaboration (CKD-EPI) equation. Physical performance was objectively measured by the SPPB. The relationship between eGFR and SPPB was investigated by multiple linear regression analysis. Physically impaired patients (SPPB total score <5) were older, had lower serum albumin and Mini-Mental State Examination (MMSE) scores as well as higher overall co-morbidity, prevalence of stroke, cancer, and anemia compared to those with intermediate (SPPB = 5–8) and good physical performance (SPPB = 9–12). Fully adjusted multivariate models showed that eGFR (modeled as 10 mL/min per 1.73 m² intervals) was independently associated with the SPPB total score ($B = 0.49$; 95% confidence interval [CI] = 0.18–0.66; $p = 0.003$), balance ($B = 0.30$; 95% CI = 0.10–0.49; $p = 0.005$), and muscle strength ($B = 0.06$; 95% CI = 0.01–0.10; $p = 0.043$), but not with walking speed ($B = -0.04$; 95% CI = -0.09 – -0.11 ; $p = 0.107$). In conclusion, reduced renal function is associated with poorer physical performance in older hospitalized patients. SPPB is worthy of testing to monitor changes in physical performance in elderly CKD patients.

Introduction

CHRONIC KIDNEY DISEASE (CKD) is highly prevalent in older adults¹ and predicts negative health outcomes, including loss of personal independence,^{2,3} hospitalization,⁴ and death.^{4–8} CKD is commonly associated with disabling chronic diseases, such as congestive heart failure, coronary artery disease, peripheral arterial disease, diabetes mellitus, and chronic obstructive pulmonary disease,^{6,9,10} and it has

been shown to independently predict incident disability in community-dwelling older persons^{3,11} and to be associated with the development of cognitive and physical impairment.^{2,12} At present, the exact mechanisms explaining the relationship between CKD and physical performance are unknown; however, studies have indicated that the heightened inflammatory state in CKD may play a pivotal role.²

A low estimated glomerular filtration rate (eGFR) is known to be associated with lower scores in subjective

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physical function and physical activity scales,^{13–15} and several former studies have demonstrated an association between renal function and objectively measured exercise capacity or physical performance.^{16–18} Considering that objective measures of physical performance can predict disability in several chronic conditions,^{19–21} these measures might also improve the management of older CKD patients. Furthermore, functional limitation frequently precedes disability and could in itself negatively affect quality of life, morbidity, and ultimately survival.^{22,23} Nevertheless, the assessment of physical performance does not yet form part of the routine clinical monitoring of CKD patients.²³

Objective measures of lower extremity physical performance have shown to be effective predictors of overall health status, functional trajectories, and death in different settings and populations.^{21,24–29} These instruments measure a performance that depends variably upon muscle and non-muscular factors. The Short Physical Performance Battery (SPPB) explores three abilities (gait speed, muscle strength, balance), does not require submaximal effort, but is largely dependent upon balance and lower extremity strength.²⁴ Recently, SPPB has been shown to predict incident disability and death in older patients following discharge from acute care hospitals.^{20,30}

In CKD, SPPB has been used to compare physical performance of CKD patients and patients with other chronic diseases,³¹ and it has been considered as primary outcome measure in a recent randomized pilot trial of resistance training during maintenance dialysis.³² However, the relationship between renal function and SPPB performance has never been formally assessed in older hospitalized adults. Investigating this relationship might help to clarify to which extent CKD contributes to physical impairment following an acute hospital admission. Therefore, we planned this analysis to pursue such an objective.

Methods

Study design and data collection

The present study used data from a collaborative multicenter study, the Pharmacovigilance in the elderly Care (PVC), based in community and university hospitals throughout Italy and aimed at surveying drug consumption, occurrence of adverse drug reactions, and quality of hospital care.^{33,34} The methods of the PVC study have been described previously.^{33,34} Briefly, all patients consecutively admitted to 11 acute care medical wards and 3 long-term care/rehabilitation units from April 1st to June 30th of 2007 were invited to participate in the study. After obtaining a written informed consent, a study physician with specific training completed a questionnaire for each patient at the moment of hospital admission that was then updated on a daily basis. A training session was carried out at the coordinating center to collect a standardized battery of tests and has been previously described.³³

Data collection included demographics, socioeconomic and clinical information, and, in particular, information regarding pharmacological therapy, along with a comprehensive geriatric assessment. Once discharged, patients were followed up every 3 months for 1 year. All patients and/or their relatives/caregivers were contacted by telephone to program every follow-up visit. At each follow-up visit, in-

formation was collected on vital status, functional status (activities of daily living [ADL]), changes in drugs prescriptions, and occurrence of adverse drug reactions (ADRs).³⁵ For this study, we used only cross-sectional data collected during hospital stay.

Overall, 762 patients were initially screened for the survey period, and 72 (9.4%) refused to participate. We also excluded 25 patients who died during the hospital stay, patients enrolled in long-term care/rehabilitation units ($n=159$), and those with missing data on serum creatinine concentrations ($n=20$); thus, our final study population consisted of 486 patients. The study protocol was approved by the Ethical Committee of the Italian National Research Center on Aging (INRCA), Ancona, Italy (ID SC/07/169; Ref# 206/March 05th, 2007).

Short Physical Performance Battery

Physical performance was measured by SPPB as previously reported.²⁴ The trained physicians administered all performance-based measures the day before discharge. The SPPB includes gait speed (usual time to walk 6 meters), five chair-stands test (time to rise from a chair and return to the seated position five times without using arms), and balance test (ability to stand with the feet together in the side-by-side, semitandem, and tandem positions). Time to walk 6 meters was converted using the formula suggested by Studenski et al.³⁶ A score from 0 to 4 was assigned to performance on each task. Individuals received a score of 0 for each task they were unable to complete. Bedridden patients were included in the group scoring 0 in all tasks. For time to walk 6 meters and time to complete chair-stands, test scores of 1 to 4 were assigned based on quartiles of performance measured in enrolled patients, as previously reported. For the balance test, the side-by-side stand, semitandem stand, and full tandem stand were considered hierarchical in difficulty and assigned a score of 1–4 on the basis of the most complex task completed. Summing the three individual categorical scores, a summary performance score was created for each participant (range, 0–12), with higher scores indicating better lower body function. The SPPB total score was categorized as 0–4, 5–8, and 9–12.²⁴

Estimated glomerular filtration rate

Serum creatinine was measured in stable condition (*i.e.*, at the time of discharge) by the standardized Jaffé method in all laboratories of participating centers. Renal function was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)³⁷ equation:

$$\begin{aligned} \text{Female} \quad & (\text{Scr} \leq 0.7) \text{ eGFR} = 144 \times (\text{Scr}/0.7)^{-0.329} \times (0.993)^{\text{Age}} \\ & (\text{Scr} > 0.7) \text{ eGFR} = 144 \times (\text{Scr}/0.7)^{-1.209} \times (0.993)^{\text{Age}} \\ \text{Male} \quad & (\text{Scr} \leq 0.9) \text{ eGFR} = 141 \times (\text{Scr}/0.9)^{-0.411} \times (0.993)^{\text{Age}} \\ & (\text{Scr} > 0.9) \text{ eGFR} = 141 \times (\text{Scr}/0.9)^{-1.209} \times (0.993)^{\text{Age}} \end{aligned}$$

The CKD-EPI equation has shown to perform slightly better than Modification of Diet in Renal Disease (MDRD) and Cockcroft–Gault (CG)-derived measures when stratifying prognosis⁸ and predicting adverse drug reactions³⁸ in elderly hospitalized patients. Participants were grouped into three categories according to their estimated eGFR (mL/min per 1.73 m²) as follows: ≥ 60 , 45–59.9, 30–44.9 (Fig. 1), and ≤ 30 . An estimated eGFR ≥ 60 mL/min per 1.73 m² was considered the reference group.

FIG. 1. Prevalence of Short Physical Performance Battery (SPPB) performance categories across estimated glomerular filtration (eGFR) groups.

Covariates

Age, gender, and nutritional indices, including body mass index (BMI) and serum albumin, were considered in the analysis. Comprehensive geriatric assessment carried out the day before discharge included: Cognitive status (Mini-Mental State Examination [MMSE]),³⁹ mood (Geriatric Depression Scale [GDS]),⁴⁰ co-morbidity (Cumulative Illness Rating Scale [CIRS]),⁴¹ and self-reported functional status (basic activities of daily living [BADL] and instrumental activities of daily living [IADL]). Selected co-morbidities known to affect physical performance and/or renal function, including arterial hypertension, diabetes, coronary artery disease, atrial fibrillation, congestive heart failure, stroke, peripheral vascular disease, chronic obstructive pulmonary disease (COPD), cancer, and anemia were separately considered in the analyses.

Analytic approach

For descriptive purpose, demographic and clinical characteristics of the study sample were compared according to SPPB categories. We used one-way analysis of variance (ANOVA) for continuous variables with the Scheffé *post hoc* test when appropriate and the Pearson chi-squared for categorical ones. Therefore, age, gender, and variables significantly associated with SPPB score in descriptive analyses were entered into a multivariable linear regression model to obtain estimate of independent correlates of SPPB total score after adjusting for potential confounders. Additional analyses were repeated with separate tasks of the SPPB as dependent variables. Finally, analyses of covariance (ANCOVA) were performed with total SPPB, muscle strength, balance, and walking speed as dependent variables in separate models controlling for potential con-

founders. Dunnett *post hoc* analysis was performed to test the strength of the associations of eGFR categories with dependent variables considering $\text{GFR} \geq 60 \text{ mL/min per } 1.73 \text{ m}^2$ as a reference category. All analyses were performed using SPSS Statistical Software Package for Windows V10.0.

Results

General characteristics and renal function of patients divided according to SPPB total score are shown in Table 1. Physically impaired patients were older, had lower serum albumin and MMSE scores, as well as higher overall co-morbidity, prevalence of stroke, cancer, and anemia. The prevalence of severe SPPB-based physical impairment was 19.3% among patients with self-rated independency in all BADLs at discharge and 9.6% among patients with self-rated independency in all IADLs at discharge. Patients with lower SPPB scores had lower average eGFR values. Interestingly, the intermediate SPPB group had significantly lower eGFR when compared with the best SPPB group ($p=0.005$) (Table 1).

The prevalence of SPPB performance categories across eGFR groups is reported in Fig. 1. Eighty-one out of 486 (16.1%) patients had a SPPB score of 0, and 50 out of the 81 were bedridden. Thus, bedridden patients accounted for 24.9% of patients being severely physically impaired (*i.e.*, of patients scoring from 0 to 4 at SPPB examination). The prevalence of severe physical impairment (SPPB score=0–4) was 62.0% among patients with $\text{eGFR} < 30 \text{ mL/min per } 1.73 \text{ m}^2$, 44.0% among patients with $\text{GFR} = 30\text{--}59.9 \text{ mL/min per } 1.73 \text{ m}^2$, and 34.5% among patients with $\text{GFR} \geq 60 \text{ mL/min per } 1.73 \text{ m}^2$ ($p < 0.001$) (Fig. 1).

Multivariate models testing adjusted for age, gender, serum albumin, MMSE, and overall co-morbidity showed that eGFR was independently associated with the SPPB total score. When the analysis was repeated considering stroke, cancer, and anemia instead of cumulative co-morbidity, the strength of the association was reduced, but it still remained statistically significant. When considering single test tasks of the SPPB as dependent variables, eGFR was significantly associated with balance and muscle strength, but not with walking speed (Table 2).

Based on adjusted ANCOVA analysis, the independent associations of severe or moderate renal dysfunction with total SPPB and its individual tasks having that of preserved renal function as reference association are shown in Table 3. Patients with the $\text{eGFR} = 30.0\text{--}45.9 \text{ mL/min per } 1.73 \text{ m}^2$ scored on average almost 1 SPPB point less than patients with normal renal function, whereas patients with $\text{eGFR} < 30 \text{ mL/min per } 1.73 \text{ m}^2$ scored about 2 SPPB points less than patients with $\text{eGFR} < 60 \text{ mL/min per } 1.73 \text{ m}^2$. A significant trend for reducing performance across eGFR categories was observed for muscle strength and balance, but only the latter was definitely depressed yet in the $\text{GFR} = 30\text{--}44.9 \text{ mL/min per } 1.73 \text{ m}^2$ category.

Discussion

Our study shows that reduced renal function is associated with poorer physical performance, as assessed by the SPPB, in older hospitalized patients. With regard to individual components of SPPB, this association persisted for muscle

TABLE 1. GENERAL CHARACTERISTICS OF PATIENTS ACROSS SHORT PHYSICAL PERFORMANCE BATTERY TOTAL SCORE CATEGORIES

	<i>All patients</i> n=486	<i>SPPB score</i>			p
		0–4 n=201	5–8 n=168	9–12 n=117	
Age (years)	80.1±6.0	82.4±6.3	79.6±5.1*	76.7±4.6*	0.001
Gender, female (n, %)	263 (54.1)	119 (59.2)	94 (56.0)	50 (42.7)	0.015
BMI (kg/m ²)	25.2±4.2	25.3±5.0	24.6±3.7	25.7±3.4	0.108
Serum albumin (g/dL)	3.6±0.7	3.4±0.8	3.7±0.5*	3.8±0.4*	0.001
MMSE score	20.5±8.9	15.3±10.5	23.9±4.8*	24.5±5.5*	0.001
GDS score	4.7±4.1	4.6±4.5	5.2±3.9	4.2±3.8	0.123
CIRS co-morbidity	3.7±1.9	4.1±1.9	3.5±1.9**	3.3±1.6*	0.001
BADL independency	331 (68.1)	64 (31.8)	153 (91.1)	114 (97.4)	0.001
IADL independency	52 (10.7)	5 (2.5)	28 (16.7)	19 (16.2)	0.001
Hypertension	346 (71.2)	134 (66.7)	128 (76.2)	84 (71.8)	0.130
Diabetes	124 (25.5)	52 (25.9)	46 (27.4)	26 (22.2)	0.610
Coronary artery disease	142 (29.2)	54 (26.9)	55 (32.7)	33 (28.2)	0.449
Atrial fibrillation	79 (16.3)	36 (17.9)	26 (15.5)	17 (14.5)	0.692
Congestive heart failure	107 (22.0)	49 (24.4)	35 (20.8)	23 (19.7)	0.557
Stroke	65 (13.4)	44 (21.9)	19 (11.3)	2 (1.7)	0.001
Peripheral vascular disease	114 (23.5)	52 (25.9)	36 (21.4)	26 (22.2)	0.567
COPD	175 (36.0)	74 (36.8)	61 (36.3)	40 (34.2)	0.631
Cancer	46 (9.5)	27 (13.4)	14 (8.3)	5 (4.3)	0.022
Anemia	190 (39.1)	103 (51.2)	63 (37.5)	24 (20.5)	0.001
SPPB score	5.2±3.6	1.4±1.5	6.3±1.2*	9.9±0.8* [#]	0.001
eGFR (mL/min per 1.73 m ²)	57.0±21.0	53.2±22.4	56.4±20.1	64.4±17.9* ^{##}	0.001

p*<0.001, *p*<0.01 vs. SPPB 0–4; #*p*<0.001, ##*p*<0.01 vs. SPPB 5–8.

SPPB, Short Physical Performance Battery; BMI, body mass index; MMSE, Mini Mental State Examination; GDS, Geriatric Depression Scale; CIRS, Cumulative Illness Rating Scale; BADL, Basic Activities of Daily Living; IADL, Instrumental Activities of Daily Living; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate.

strength and balance, but not for walking speed, after adjusting for demographic and clinical variables.

Studies have shown individuals with end-stage renal disease have significantly lower physical functioning compared to the general population,⁴² as well as in comparison to those with other common chronic diseases, such as diastolic heart failure, chronic obstructive pulmonary disease, or at high risk for cardiovascular disease.³¹ Our data confirmed that patients with reduced renal function (eGFR levels=30–45.9 mL/min per 1.73 m²) were more likely to have poorer total physical performance and had on average almost 1 SPPB point less than patients with levels of eGFR≥60 mL/min per 1.73 m². These findings seem of interest when considering that physical functioning strongly predicts morbidity and mortality in community-dwelling older adults.^{25,43,44} Furthermore, measures of physical function in the clinical practice have been proposed as screening “vital signs” for the risk of falls, hospitalization, and mortality in older adults, but only recently has interest for the use of these measures in a hospital setting. In particular, SPPB was found to be a valid indicator of functional and clinical status⁴⁵ and to predict prognosis in older acute care inpatients.^{20,30} The present study is the first one showing that SPPB correlates strictly with renal function in older inpatients. This finding is of special interest because the studied population was plagued with important co-morbidity apt to weaken or conceal the SPPB–eGFR association.

Current evidence suggests that using objective measures of physical performance may help to identify early signs of

disability,¹⁹ and a not negligible proportion of patients with self-rated independency at BADL/IADL was found to be physically impaired at SPPB measurement. For instance, SPPB has been shown to be highly predictive of falls,⁴⁶ which, in turn mark a dramatic decline of personal independence through a variety of mechanisms.⁴⁷ Furthermore, SPPB can reveal slowing of walking, which is the hallmark of highly disabling conditions, such as Parkinson disease, deconditioning, arthritis, and other medical co-morbidities (e.g., hypothyroidism), and predicts further decline in functioning.^{48,49} Finally, the inverse relationship between SPPB score and functional decline observed in previous studies suggests that SPPB captures a dimension of physical performance that could be helpful in defining the risk of further physical decline in older patients.^{19,20,24,50} Our study suggests that a similar conclusion applies to CKD-related physical impairment, but a confirmatory prospective study is needed.

There may be several mechanisms explaining the CKD-related impairment in physical performance of older patients. Sarcopenia, defined as a loss of muscle mass with limited mobility,⁵¹ is a common finding in older adults, and its prevalence rises sharply with declining kidney function in adults.⁵² Furthermore, it is widely known that inflammatory markers are elevated during CKD,^{2,53} and higher levels of interleukin-6 (IL-6) have been associated with incident mobility disability in older adults, perhaps due to a decline in muscle strength. Indeed, it has been suggested that inflammation mediates the association between CKD and functional limitation in older community-dwelling adults.²

TABLE 2. MULTIVARIABLE LINEAR REGRESSION MODELS TO SHORT PHYSICAL PERFORMANCE BATTERY TOTAL SCORE AND INDIVIDUAL PERFORMANCE TASKS

	SPPB total score (range 0–12)			Walking speed (range 0–4)			Muscle strength (range 0–4)			Balance (range 0–4)		
	Adj R ² = 0.43			Adj R ² = 0.27			Adj R ² = 0.28			Adj R ² = 0.42		
	B	95% CI	p	B	95% CI	p	B	95% CI	p	B	95% CI	p
Age (years)	–0.14	–0.19; –0.09	0.001	–0.05	–0.06; –0.03	0.001	–0.02	–0.04; –0.01	0.011	–0.05	–0.07; –0.03	0.001
Gender (female)	–0.71	–1.26; –0.14	0.013	–0.21	–0.41; –0.01	0.041	–0.48	–0.70; –0.26	0.001	–0.31	–0.54; –0.06	0.006
Serum albumin (g/dL)	0.80	0.37; 1.23	0.001	0.34	0.19; 0.49	0.001	0.41	0.24; 0.58	0.001	0.46	0.29; 0.62	0.001
MMSE (total score)	0.16	0.13; 0.20	0.001	0.04	0.03; 0.05	0.001	0.05	0.03; 0.06	0.001	0.07	0.06; 0.09	0.001
CIRS co-morbidity, score	–0.30	–0.46; –0.15	0.001	–0.05	–0.10; –0.01	0.092	–0.10	–0.15; –0.03	0.003	–0.11	–0.18; –0.05	0.001
eGFR* (mL/min per 1.73 m ²)	0.49	0.18; 0.66	0.003	–0.04	–0.09; 0.11	0.107	0.06	0.01; 0.10	0.043	0.30	0.10; 0.49	0.005
Adj R ² = 0.46												
Adj R ² = 0.29												
Adj R ² = 0.26												
Adj R ² = 0.44												
Age (years)	–0.13	–0.18; –0.08	0.001	–0.04	–0.06; –0.02	0.001	–0.02	–0.04; –0.01	0.020	–0.05	–0.07; –0.03	0.001
Gender (female)	–0.56	–1.11; –0.02	0.043	–0.22	–0.41; –0.02	0.031	–0.45	–0.66; –0.23	0.001	–0.30	–0.52; –0.08	0.008
Serum albumin (g/dL)	0.78	0.35; 1.21	0.001	0.27	0.11; 0.42	0.001	0.39	0.21; 0.56	0.001	0.39	0.21; 0.56	0.001
MMSE score	0.15	0.12; 0.18	0.001	0.04	0.03; 0.05	0.001	0.04	0.03; 0.05	0.001	0.07	0.06; 0.08	0.001
Stroke	–1.61	–2.43; –0.78	0.001	–0.25	–0.53; –0.03	0.028	–0.56	–0.87; –0.25	0.001	–0.51	–0.82; –0.20	0.001
Cancer	–0.45	–1.41; 0.50	0.352	–0.22	–0.54; 0.10	0.169	0.12	–0.23; 0.48	0.494	–0.34	–0.69; 0.02	0.064
Anemia	–0.84	–1.44; –0.25	0.006	–0.38	–0.59; –0.17	0.001	–0.27	–0.51; –0.04	0.024	–0.43	–0.66; –0.19	0.001
eGFR* mL/min per 1.73 m ²	0.28	0.09; 0.61	0.008	–0.04	–0.09; 0.01	0.101	0.05	0.01; 0.10	0.048	0.28	0.09; 0.57	0.008

B values were calculated for each 10 mL/min per 1.73 m² intervals.

SBBP, Short Physical Performance Battery; CI, confidence interval; MMSE, Mini-Mental State Examination; eGFR, estimated glomerular filtration rate.

TABLE 3. ANCOVA MODELS TESTING THE RELATIONSHIP OF ESTIMATED GLOMERULAR FILTRATION RATE CATEGORIES TO SHORT PHYSICAL PERFORMANCE BATTERY TOTAL SCORE AND INDIVIDUAL PERFORMANCE TASKS

<i>SPPB total score (range 0–12)</i>			
	<i>Mean difference</i>	<i>95% CI</i>	<i>p</i>
eGFR, mL/min per 1.73 m ²			
≥60	Ref.		
45.0–59.9	–0.57	–1.51; 0.37	0.371
30.0–44.9	–1.28	–2.37; –0.18	0.016
<30	–2.26	–3.60; –0.93	0.001
<i>Walking speed score (range 0–4)</i>			
	<i>Mean difference</i>	<i>95% CI</i>	<i>P</i>
≥60	Ref.		
45.0–59.9	–0.06	–0.42; 0.30	0.964
30.0–44.9	–0.38	–0.80; 0.03	0.080
<30	–0.47	–0.98; 0.03	0.075
<i>Muscle strength score (range 0–4)</i>			
	<i>Mean difference</i>	<i>95% CI</i>	<i>p</i>
≥60	Ref.		
45.0–59.9	–0.24	–0.62; 0.14	0.343
30.0–44.9	–0.26	–0.70; 0.18	0.398
<30	–0.76	–1.30; –0.22	0.002
<i>Balance score (range 0–4)</i>			
	<i>Mean difference</i>	<i>95% CI</i>	<i>p</i>
≥60	Ref.		
45.0–59.9	–0.27	–0.69; 0.16	0.332
30.0–44.9	–0.63	–1.12; –0.14	0.007
<30	–1.03	–1.63; –0.43	0.001

Models adjusted for age, gender, serum albumin, MMSE, and overall co-morbidity.

ANCOVA, Analysis of covariance; SPPB, Short Physical Performance Battery; CI, confidence interval; eGFR, estimated glomerular filtration rate.

Surprisingly, the relationship between kidney function and walking speed, a subtask equivalent or even superior to SPPB according to recent studies⁵⁴ in identifying patients at risk of disability or death,³⁶ was not significant in this study. In our multivariate models, total eGFR levels were associated with muscle strength and balance, but not with walking speed. In detail, when eGFR category levels were considered, we found that patients with significantly reduced renal function (GFR <30 mL/min per 1.73 m²) were approximately 1.5 more likely to have lower scores on muscle strength and balance tasks compared to those with normal renal function. Also moderate renal dysfunction (eGFR = 30.0–59.9 mL/min per 1.73 m²) was associated with lower odds of having a better performance on muscle strength and balance tasks. On the contrary, no category of eGFR was associated with walking speed. This finding may highlight that walking speed in the hospital setting is less informative than in well-functioning community dwelling elders.

Selected nutrient deficits might underlie the relationship between renal function and balance. Indeed, vitamin D

deficiency, which is highly prevalent among elders, may predispose to osteoporosis and related complications, such as vertebral fractures⁵⁵ and, then, postural instability. Furthermore, vitamin D deficit preferentially weakens hip and thigh muscles, which are primarily involved in dynamic balance.⁵⁶ Interestingly, it has been recently demonstrated that vitamin D supplementation in CKD patients with vitamin D deficit improved muscle strength, functional ability, and balance.⁵⁷ Additionally, vitamin B12 and folic acid deficiency, which are highly prevalent among CKD patients, could also contribute to bone loss,⁵⁸ postural instability, and increased risk of falls as well as peripheral neuropathy and subcortical encephalopathy, both common in elderly CKD patients.⁵⁹

The relationship between renal function and muscle strength likely reflects renal failure-related sarcopenia. SPPB scores for muscle strength were associated with lower serum albumin, and low serum albumin levels, even within the normal range, were independently associated with weaker muscle strength and future decline in muscle strength in older people.⁶⁰ Similarly, anemia, another correlate of lower SPPB score for muscle strength, was also associated with lower knee extensor and handgrip strength in community-dwelling older subjects.⁶¹

This study has many limitations. First, it lacked a direct measurement of GFR or other markers of renal function, such as cystatin C. Second, being cross-sectional, it does not clarify to which extent renal function can predict incident physical impairment. Third, because of its limited power, it may lack precision in estimates of the associations observed. Such a limitation could explain the lack of significant association between eGFR and walking speed. Fourth, the lack of information on muscle mass and chronic inflammatory cytokines limits our insight into the mechanisms underlying the observed relationships. Finally, eGFR might to some extent be underestimated due to the hypercatabolic state secondary to the acute illness or be truly depressed in the context of acute and not chronic renal failure. However, having measured serum creatinine in stable clinical conditions likely reduced the size of this problem.

In conclusion, our study shows that reduced renal function is associated with poorer physical performance, objectively rated by SPPB, in elderly hospitalized patients. Our results suggest that impaired muscle strength and balance may be the hallmark of elderly patients with CKD. In instances of frequent impairment despite preserved BADLs/IADLs, SPPB could be helpful in defining the CKD-related profile of physical impairment, but only prospective observational studies could clarify the prognostic implications of SSPB with regard to personal independence, as well as to the evolution of renal disease. Indeed, if determinants of abnormal SPPB performance were strictly related to chronic renal failure, as it seems very likely, SPPB would qualify as an index of CKD severity and, as such, might expand our set of predictors of this heterogeneous condition. Thus, SPPB seems worthy of exploration as a low-cost and very promising assessment instrument for elderly CKD patients.

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Author Disclosure Statement

All Authors declare they have no conflict of interest regarding this manuscript.

References

- Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA* 2007;298:2038–2047.
- Fried LF, Lee JS, Shlipak M, et al. Chronic kidney disease and functional limitation in older people: Health, aging and body composition study. *J Am Geriatr Soc* 2006;54:750–756.
- Pedone C, Corsonello A, Bandinelli S, et al. Relationship between renal function and functional decline: Role of the estimating equation. *J Am Med Dir Assoc* 2012;13:84 e11–e84.
- Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351:1296–1305.
- Mahon NG, Blackstone EH, Francis GS, et al. The prognostic value of estimated creatinine clearance alongside functional capacity in ambulatory patients with chronic congestive heart failure. *J Am Coll Cardiol* 2002;40:1106–1113.
- McAlister FA, Ezekowitz J, Tonelli M, Armstrong PW. Renal insufficiency and heart failure: Prognostic and therapeutic implications from a prospective cohort study. *Circulation* 2004;109:1004–1009.
- Corsonello A, Pedone C, Lattanzio F, et al. Does concealed chronic kidney disease predict survival of older patients discharged from acute care hospitals? *Rejuvenation Res* 2010;13:539–545.
- Corsonello A, Pedone C, Lattanzio F, et al. Chronic kidney disease and 1-year survival in elderly patients discharged from acute care hospitals: A comparison of three glomerular filtration rate equations. *Nephrol Dial Transplant* 2011;26:360–364.
- Joseph J, Koka M, Aronow WS. Prevalence of moderate and severe renal insufficiency in older persons with hypertension, diabetes mellitus, coronary artery disease, peripheral arterial disease, ischemic stroke, or congestive heart failure in an academic nursing home. *J Am Med Dir Assoc* 2008;9:257–259.
- Incalzi RA, Corsonello A, Pedone C, et al. Chronic renal failure: A neglected comorbidity of COPD. *Chest* 2009;137:831–827.
- Plantinga LC, Johansen K, Crews DC, et al. Association of CKD with disability in the United States. *Am J Kidney Dis* 2011;57:212–227.
- Khatrri M, Nickolas T, Moon YP, et al. CKD associates with cognitive decline. *J Am Soc Nephrol* 2009;20:2427–2432.
- Lin J, Curhan GC. Kidney function decline and physical function in women. *Nephrol Dial Transplant* 2008;23:2827–2833.
- Johansen KL, Kaysen GA, Young BS, et al. Longitudinal study of nutritional status, body composition, and physical function in hemodialysis patients. *Am J Clin Nutr* 2003;77:842–846.
- Kurella M, Ireland C, Hlatky MA, et al. Physical and sexual function in women with chronic kidney disease. *Am J Kidney Dis* 2004;43:868–876.
- Odden MC, Whooley MA, Shlipak MG. Association of chronic kidney disease and anemia with physical capacity: The heart and soul study. *J Am Soc Nephrol* 2004;15:2908–2915.
- Odden MC, Chertow GM, Fried LF, et al. Cystatin C and measures of physical function in elderly adults: the Health, Aging, and Body Composition (HABC) Study. *Am J Epidemiol* 2006;164:1180–1189.
- McManus D, Shlipak M, Ix JH, et al. Association of cystatin C with poor exercise capacity and heart rate recovery: Data from the heart and soul study. *Am J Kidney Dis* 2007;49:365–372.
- Guralnik JM, Ferrucci L, Simonsick EM, et al. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* 1995;332:556–561.
- Corsonello A, Lattanzio F, Pedone C, et al. Prognostic significance of the Short Physical Performance Battery in older patients discharged from acute care hospitals. *Rejuvenation Res* 2012;15:41–48.
- Chiarantini D, Volpato S, Sioulis F, et al. Lower extremity performance measures predict long-term prognosis in older patients hospitalized for heart failure. *J Card Fail* 2010;16:390–395.
- Painter P, Johansen KL. Improving physical functioning: Time to be a part of routine care. *Am J Kidney Dis* 2006;48:167–170.
- Koufaki P, Mercer T. Assessment and monitoring of physical function for people with CKD. *Adv Chronic Kidney Dis* 2009;16:410–419.
- 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.
- Rolland Y, Lauwers-Cances V, Cesari M, et al. Physical performance measures as predictors of mortality in a cohort of community-dwelling older French women. *Eur J Epidemiol* 2006;21:113–122.
- 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.
- Cooper R, Kuh D, Hardy R. Objectively measured physical capability levels and mortality: Systematic review and meta-analysis. *BMJ* 2010;341:c4467.
- Blain H, Carriere I, Sourial N, et al. Balance and walking speed predict subsequent 8-year mortality independently of current and intermediate events in well-functioning women aged 75 years and older. *J Nutr Health Aging* 2010;14:595–600.
- Klepin HD, Geiger AM, Tooze JA, et al. Physical performance and subsequent disability and survival in older adults with malignancy: results from the health, aging and body composition study. *J Am Geriatr Soc* 2010;58:76–82.
- Volpato S, Cavalieri M, Sioulis F, et al. Predictive value of the Short Physical Performance Battery following hospitalization in older patients. *J Gerontol A Biol Sci Med Sci* 2011;66:89–96.
- Hartmann EL, Kitzman D, Rocco M, et al. Physical function in older candidates for renal transplantation: An impaired population. *Clin J Am Soc Nephrol* 2009;4:588–594.
- Chen JL, Godfrey S, Ng TT, et al. Effect of intra-dialytic, low-intensity strength training on functional capacity in adult

- haemodialysis patients: A randomized pilot trial. *Nephrol Dial Transplant* 2010;25:1936–1943.
33. Corsonello A, Pedone C, Lattanzio F, et al. Potentially inappropriate medications and functional decline in elderly hospitalized patients. *J Am Geriatr Soc* 2009;57:1007–1014.
 34. Corsonello A, Pedone C, Lattanzio F, et al. Regimen complexity and medication nonadherence in elderly patients. *Ther Clin Risk Manag* 2009;5:209–216.
 35. World Health Organization. International Drug Monitoring: The Role of the Hospital. Technical Report Series No. 425. World Health Organization, Geneva, Switzerland, 1969.
 36. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011;305:50–58.
 37. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604–612.
 38. Corsonello A, Pedone C, Lattanzio F, et al. Association between glomerular filtration rate and adverse drug reactions in elderly hospitalized patients: The role of the estimating equation. *Drugs Aging* 2011;28:379–390.
 39. 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.
 40. Lesher EL, Berryhill JS. Validation of the Geriatric Depression Scale–Short Form among inpatients. *J Clin Psychol* 1994;50:256–260.
 41. Conwell Y, Forbes NT, Cox C, Caine ED. Validation of a measure of physical illness burden at autopsy: The Cumulative Illness Rating Scale. *J Am Geriatr Soc* 1993;41:38–41.
 42. Singer MA, Hopman WM, MacKenzie TA. Physical functioning and mental health in patients with chronic medical conditions. *Qual Life Res* 1999;8:687–691.
 43. Sui X, Laditka JN, Hardin JW, Blair SN. Estimated functional capacity predicts mortality in older adults. *J Am Geriatr Soc* 2007;55:1940–1947.
 44. Newman AB, Simonsick EM, Naydeck BL, et al. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. *JAMA* 2006;295:2018–2026.
 45. Volpato S, Cavalieri M, Guerra G, et al. Performance-based functional assessment in older hospitalized patients: feasibility and clinical correlates. *J Gerontol A Biol Sci Med Sci* 2008;63:1393–1398.
 46. Quadri P, Tettamanti M, Bernasconi S, et al. Lower limb function as predictor of falls and loss of mobility with social repercussions one year after discharge among elderly inpatients. *Aging Clin Exp Res* 2005;17:82–89.
 47. Finlayson ML, Peterson EW. Falls, aging, and disability. *Phys Med Rehabil Clin N Am* 2010;21:357–373.
 48. Louis ED, Bennett DA. Mild Parkinsonian signs: An overview of an emerging concept. *Mov Disord* 2007;22:1681–1688.
 49. Inzitari M, Pozzi C, Ferrucci L, et al. Subtle neurological abnormalities as risk factors for cognitive and functional decline, cerebrovascular events, and mortality in older community-dwelling adults. *Arch Intern Med* 2008;168:1270–1276.
 50. Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. *J Am Geriatr Soc* 2003;51:314–322.
 51. Morley JE, Abbatecola AM, Argiles JM, et al. Sarcopenia with limited mobility: an international consensus. *J Am Med Dir Assoc* 2011;12:403–409.
 52. Foley RN, Wang C, Ishani A, et al. Kidney function and sarcopenia in the United States general population: NHANES III. *Am J Nephrol* 2007;27:279–286.
 53. Shlipak MG, Stehman-Breen C, Fried LF, et al. The presence of frailty in elderly persons with chronic renal insufficiency. *Am J Kidney Dis* 2004;43:861–867.
 54. Cesari M. Role of gait speed in the assessment of older patients. *JAMA* 2011;305:93–94.
 55. Cesari M, Incalzi RA, Zamboni V, Pahor M. Vitamin D hormone: A multitude of actions potentially influencing the physical function decline in older persons. *Geriatr Gerontol Int* 2011;11:133–142.
 56. Bischoff-Ferrari HA, Conzelmann M, Stahelin HB, et al. Is fall prevention by vitamin D mediated by a change in postural or dynamic balance? *Osteoporos Int* 2006;17:656–663.
 57. Taskapan H, Baysal O, Karahan D, et al. Vitamin D and muscle strength, functional ability and balance in peritoneal dialysis patients with vitamin D deficiency. *Clin Nephrol* 2011;76:110–116.
 58. Golbahar J, Hamidi A, Aminzadeh MA, Omrani GR. Association of plasma folate, plasma total homocysteine, but not methylenetetrahydrofolate reductase C667T polymorphism, with bone mineral density in postmenopausal Iranian women: A cross-sectional study. *Bone* 2004;35:760–765.
 59. Krishnan AV, Kiernan MC. Neurological complications of chronic kidney disease. *Nat Rev Neurol* 2009;5:542–551.
 60. Schalk BW, Deeg DJ, Penninx BW, et al. Serum albumin and muscle strength: A longitudinal study in older men and women. *J Am Geriatr Soc* 2005;53:1331–1338.
 61. Penninx BW, Pahor M, Cesari M, et al. Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. *J Am Geriatr Soc* 2004;52:719–724.

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