

## A functional tool demonstrating the physical function decline independent of age in patients with predialysis chronic kidney disease

Özlem TAŞOĞLU<sup>1\*</sup>, Nergiz BAYRAKCI<sup>2</sup>, Didem SEZGİN ÖZCAN<sup>1</sup>, Nihal ÖZKAYAR<sup>3</sup>, İrfan TAŞOĞLU<sup>4</sup>, Neşe ÖZGİRİN<sup>1</sup>

<sup>1</sup>Ankara Physical Medicine and Rehabilitation Training and Research Hospital, Ankara, Turkey

<sup>2</sup>Department of Nephrology, Ankara Numune Training and Research Hospital, Ankara, Turkey

<sup>3</sup>Department of Nephrology, Faculty of Medicine, Hitit University, Çorum, Turkey

<sup>4</sup>Department of Cardiovascular Surgery, Ankara Yüksek İhtisas Training and Research Hospital, Ankara, Turkey

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**Background/aim:** Physical function decline in chronic kidney disease (CKD) patients has been a popular area of investigation in the last decade. It has been shown that lower levels of physical function in CKD results in poor outcomes. Nevertheless, nephrology practice does not include routine assessment of physical function. The aim of the present study is to elucidate which physical function assessment tool is better in CKD.

**Materials and methods:** A total of 148 predialysis CKD patients and 40 healthy controls were included in this cross-sectional single-blind study. CKD patients were further divided into two groups as stage 3 and stage 4/5. A hand dynamometer, the Short Physical Performance Battery (SPPB), and the Timed Up and Go Test (TUGT) were applied to all study participants.

**Results:** All physical function tests were significantly different between study and control groups. In multivariate analysis the SPPB ( $P < 0.001$ ) emerged as an independent variable in CKD group.

**Conclusion:** The SPPB is a promising, easily applicable, inexpensive, and sensitive tool that can indicate functional decline independent of age in predialysis CKD patients and can be used in clinical practice to monitor these patients.

**Key words:** Glomerular filtration rate, hand dynamometer, Short Physical Performance Battery, Timed Up and Go Test

### 1. Introduction

It is now known that patients with chronic kidney disease (CKD) have lower levels of physical function, giving rise to poor physical activity and resulting in poor outcomes. Impaired physical performance has been associated with increased hospitalizations as well as morbidity and mortality in CKD patients (1–7). Functional decline has been found proportionally related to decrease in estimated glomerular filtration rate (eGFR) (8). Nevertheless, nephrology practice does not include assessment of physical function or an effort to prevent physical function deterioration in time on a routine basis (9).

Evaluation of physical function in CKD enables clinicians to identify patients with a high risk of morbidity/mortality, designing exercise programs to prevent worsening and provide clinical improvement, follow patients over time, and realize the deterioration/improvement of medical conditions and monitor the effectiveness of therapeutic interventions (10,11).

For use in clinical practice, assessment tools should be easily applicable, inexpensive, and sensitive to changes. Although there are many physical function tests used for CKD patients in the literature, there is not a clear consensus on which one is better to use in the clinical setting. The aim of the present study is therefore to elucidate which physical function assessment tool is better to use with CKD patients.

### 2. Materials and methods

A total of 148 consecutive patients who were admitted to the nephrology department of a training and research hospital with a diagnosis of CKD in January–October 2015 and 40 healthy controls were included in this cross-sectional study. Healthy controls were chosen from healthy hospital staff on a voluntary basis. Inclusion criteria for the patients were age between 18 and 80 years and eGFR of  $<60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$  at enrollment. Exclusion criteria included patients under dialysis treatment, acute kidney

\* Correspondence: ozlem81tasoglu@yahoo.com

injury, clinical signs of acute infection during the month preceding the inclusion, active cancer or liver disease at the time of evaluation, previous diagnosis of immunological diseases, hypothyroidism, hyperthyroidism, severe chronic obstructive pulmonary disease, severe heart failure, rheumatologic diseases including acute exacerbation of osteoarthritis, recent malignancy, neuromuscular disease, immobilization for 1 week or more during the last 3 months, orthopedic surgery during the last 1 year or still causing pain or functional limitation, inability to walk a distance of 250 m, and use of immunosuppressive drugs. Stage 1 and 2 CKD patients ( $eGFR \geq 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ ) were not included owing to the fact that metabolic complications of CKD usually become more distinct in stage 3 and over (12). This study was performed in accordance with the Declaration of Helsinki. Hospital ethics committee approval was obtained and all patients provided written informed consent.

Demographic and clinical characteristics of the participants were recorded. Routine blood tests including complete blood count and blood biochemical analysis were performed. Body mass indexes and  $eGFR$  were calculated. Patients were divided into two groups as CKD stage 3 and CKD stage 4 and 5 for further intragroup analyses. Physical function tests were performed by a blind physical medicine and rehabilitation specialist at the physical medicine and rehabilitation department of a training and research hospital.

CKD stages:

Stage 1:  $eGFR \geq 90 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$  with kidney damage (proteinuria, abnormal urinalysis, biopsy, or imaging studies).

Stage 2:  $eGFR: 60\text{--}89 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$  with kidney damage (proteinuria, abnormal urinalysis, biopsy, or imaging studies).

Stage 3:  $eGFR: 30\text{--}59 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ .

Stage 4:  $eGFR: 15\text{--}29 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ .

Stage 5:  $eGFR < 15 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ .

The measurements of grip strength were performed with a Jamar type hydraulic hand dynamometer (Sammons Preston, USA) and by the dominant hand using the American Society of Hand Therapists protocol. The patient is seated, shoulders are adducted and neutrally rotated, the elbow is flexed at  $90^\circ$ , the forearm is in a neutral position, and the wrist is between  $0^\circ$  and  $30^\circ$  dorsiflexion. The mean of three measurements was used (13). All values were recorded in kilograms.

The Short Physical Performance Battery (SPPB) was used to evaluate predominantly lower extremity function. It consists of three independent parts: chair stands, balance, and a walk of 2.44 m. Chair stands measure the ability to stand up and sit down with arms crossed on the chest 5 times. The balance test measures the ability to stand side-

by-side, semitandem, and tandem each for 10 s. The walk test measures the fastest time of two usual-pace walk trials of 2.44 m each. Each part is scored between 0 and 4, with 0 representing an inability to attempt or complete the test and 4 representing the highest level of performance. The total score is the sum of these scores and ranges between 0 and 12 (14). The SPPB was developed to evaluate lower extremity function for the Established Populations for Epidemiology Research in the Elderly cohort study for use in gerontological populations. In elderly patients the SPPB is highly predictive of death, hospitalization, and need for institutional care (15).

The Timed Up and Go Test (TUGT) was used to measure the time needed to stand up from a chair, walk 3 m, turn around, walk back, and sit down again. It is easy to perform and valuable for assessing static and dynamic balance (16).

### 2.1. Statistical analysis

Analysis was performed using SPSS 20.0 (IBM Corp., Armonk, NY, USA). Distribution of continuous variables was evaluated by Shapiro–Wilk test. Descriptive statistics were expressed as mean  $\pm$  standard deviation for continuous variables and median (minimum–maximum) for discrete variables. Categorical variables were summarized as number (n) and percentage (%). The significance of the difference between the two groups in terms of mean values was assessed with Student's t-test and median values with the Mann–Whitney U test. Chi-square analysis was used to assess the categorical variables.  $P < 0.05$  was considered statistically significant.

Variables found to be significantly different between control and CKD groups (Table 1) were evaluated by univariate analyses. Variables for which the unadjusted P-value was  $< 0.10$  in logistic regression analysis were identified as potential risk markers and included in the full model. The model was reduced using stepwise multivariate logistic regression analyses and potential markers were eliminated using likelihood ratio tests.  $P < 0.05$  was considered statistically significant and the confidence interval was 95%.

### 3. Results

Of the 188 participants included in the study, 40 (19 males, 21 females) were healthy controls and 148 (71 males, 77 females) were patients with CKD. Numbers of patients in each stage were as follows: stage 3 ( $n = 96$ ), stage 4 ( $n = 35$ ), and stage 5 ( $n = 17$ ). Demographic characteristics and physical performance tests of the patients and healthy controls are presented in Table 1. Except sex, all of the demographic characteristics and physical function tests were significantly different between study and control groups (Tables 1 and 2). In univariate analyses, age ( $P < 0.001$ ), BMI ( $P < 0.001$ ), measurement of grip strength ( $P$

**Table 1.** Demographic characteristics of the patients.

	Control group n = 40	CKD group n = 148	P
Age, mean ± SD (min–max)	39.1 ± 9.3 (24–66)	59.1 ± 11.4 (20–78)	<0.001*
Sex			
Male/female, n (%)	19 (47.5)/21 (52.5)	71(48)/77(52)	0.958
Height, mean±SD	166.77 ± 7.63	162.39 ± 8.97	0.005*
Weight, mean±SD	73.43 ± 12.47	78.27 ± 14.15	0.031*
BMI, mean±SD	26.43 ± 4.37	29.65 ± 4.75	<0.001*

\*:P < 0.05, significant. CKD: Chronic kidney disease, BMI: body mass index, SPPB: Short Physical Performance Battery, TUGT: Timed Up and Go Test.

**Table 2.** Physical performance test results of the patients.

	Control group n = 40	CKD group n = 148	P
Dynamometer, mean ± SD			
Male	39.55 ± 9.18	33.59 ± 7.72	0.005*
Female	27.36 ± 6.17	19.84 ± 6.18	<0.001*
SPPB, median (min–max)			
Male Chair stands	4 (3–4)	4 (2–4)	0.001*
Balance test	4 (4–4)	4 (2–4)	0.012*
Walk test	4 (4–4)	4 (2–4)	0.001*
Total	12 (11–12)	11 (8–12)	<0.001*
Female Chair stands	4 (4–4)	3 (1–4)	<0.001*
Balance test	4 (4–4)	4 (0–4)	0.001*
Walk test	4 (3–4)	3 (1–4)	<0.001*
Total	12 (11–12)	9 (4–12)	<0.001*
TUGT, mean ± SD			
Male	7.19 (4.88–10.16)	9.08 (5.28–14.59)	<0.001*
Female	7.70 (6.20–10.16)	10.84 (6.89–24.57)	<0.001*

\*:P < 0.05, significant. SD: Standard deviation, CKD: chronic kidney disease, SPPB: Short Physical Performance Battery, TUGT: Timed Up and Go Test.

< 0.001), SPPB (P < 0.001), and TUGT (P < 0.001) were statistically significant. In multiple logistic regression analyses, age (P < 0.001), BMI (P = 0.03), and SPPB (P < 0.001) emerged as independent variables in the study group (Table 3).

The patients in the study group were further analyzed to demonstrate the differences in physical function tests according to different CKD stages. Patients were divided into two groups according to CKD stages as stage 3 and stage 4/5. Except sex, there were no statistically significant differences between the demographic characteristics

of the groups (Table 4). There were also no significant differences regarding the physical function tests (Table 5).

#### 4. Discussion

The results of the present study demonstrated that the SPPB is a useful tool to assess physical function in CKD patients regardless of age and BMI. On the other hand, grip strength measurement and TUGT seem not to be as specific/sensitive as the SPPB for the evaluation of physical function in CKD.

Physical performance decline in CKD is a new area of investigation that has started to be discussed in the last 7

**Table 3.** Results of univariate and multivariate regression models.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	0.86 (0.82–0.90)	<0.001*	0.90 (0.85–0.95)	<0.001*
BMI	0.83 (0.76–0.92)	<0.001*	0.86 (0.75–0.98)	0.03*
Dynamometer	1.07 (1.03–1.11)	<0.001*	1.01 (0.94–1.07)	0.75
SPPB total	14.64 (4.45–48.11)	<0.001*	15.05 (2.92–77.46)	0.001*
TUGT	0.39 (0.27–0.55)	<0.001*	0.83 (0.52–1.33)	0.45

\*:P < 0.05, significant. BMI: Body mass index, SPPB: Short Physical Performance Battery, TUGT: Timed Up and Go Test.

**Table 4.** Demographic characteristics of CKD patients in stages 3 and 4/5.

	CKD stage 3 n = 96	CKD stage 4/5 n = 52	P
Age, mean ± SD (min–max)	59.54 ± 10.92	58.25 ± 12.37	0.514
Sex			
Male/female, n (%)	56 (58.3)/40(41.7)	15(28.8)/37(71.2)	0.001*
Height, mean ± SD	163.21 ± 8.93	160.86 ± 8.91	0.128
Weight, mean ± SD	79.81 ± 13.81	75.43 ± 14.46	0.072
BMI, mean ± SD	29.97 ± 4.79	29.06 ± 4.66	0.272

\*:P < 0.05 significant. SD: Standard deviation, CKD: chronic kidney disease, BMI: body mass index.

**Table 5.** Physical performance test results of CKD patients in stages 3 and 4/5.

	CKD stage 3 n = 96	CKD stage 4/5 n = 52	P
Dynamometer, mean ± SD			
Male	33.99 ± 7.51	32.12 ± 8.58	0.411
Female	20.31 ± 6.51	19.33 ± 5.84	0.490
SPPB, median (min–max)			
Male Chair stands	3 (2–4)	4 (2–4)	0.641
Balance test	4 (2–4)	4 (2–4)	0.842
Walk test	4 (2–4)	4 (2–4)	0.646
Total	11 (8–12)	11 (8–12)	0.436
Female Chair stands	3 (1–4)	3 (1–4)	0.638
Balance test	4 (0–4)	4 (1–4)	0.655
Walk test	3 (1–4)	3 (1–4)	0.092
Total	9 (4–12)	9 (4–12)	0.372
TUGT, mean ± SD			
Male	9.27 (5.28–14.59)	8.79 (5.96–12.40)	0.607
Female	10.43 (6.89–16.50)	11.37 (7.83–24.57)	0.092

SD: Standard deviation, CKD: chronic kidney disease, SPPB: Short Physical Performance Battery, TUGT: Timed Up and Go Test.

or 8 years. In 2008 Brodin et al. evaluated grip strength, knee extensor strength, TUGT, and rising from a 45-cm chair without using the hands in 55 predialysis patients with eGFR of  $\leq 20 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ . According to their results, there were no associations between eGFR and grip strength, knee extensor strength, and TUGT, but eGFR and rising from a 45-cm chair without using the hands were inversely correlated. For every  $1 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$  decrease in eGFR, the odds ratio was 1.5 times higher that the patient would not be able to rise from the chair. The results of that study are in concordance with ours as grip strength and TUGT were found useless for predicting the physical function decline in predialysis patients. Furthermore, as rising from a chair predominantly represents lower extremity function and is a part of the SPPB, worse results with decreasing eGFR also support our results (17).

Later on, in 2009, Okuno et al. similarly investigated the association between eGFR and physical function by using grip strength, functional reach, one leg stance, tandem stance, 5-m walk, and TUGT in 109 patients  $\geq 65$  years. Multiple linear regression analysis results suggested that eGFR was significantly associated with functional reach and tandem stance, but not TUGT and grip strength. Again, these results also confirm ours (18).

A total of 385 ambulatory, stroke-free CKD stage 2–4 patients were included in a study by Roshanravan et al. (7) in 2013. Hand-grip strength, usual gait speed, TUGT, and 6-min walking test were evaluated. All test results were 30%–39% lower in that study population compared to healthy adults. In contrast, hand-grip strength was not impaired. Moreover, the results of that study revealed that gait speed and TUGT more strongly predicted 3-year mortality in CKD than kidney function or more commonly measured serum biomarkers. These results, with worse lower extremity performance measures and relatively preserved upper extremity performance measures, are in concordance with our results to a certain extent.

In another study by Hiraki et al. in 2013, 120 predialysis stage 2–5 CKD patients were evaluated. Knee extensor muscle strength, single-leg stance time, maximum gait speed, and even hand-grip strength (in contrast to similar studies) were all decreased with the progression of CKD and all physical function tests showed positive correlations with eGFR. Additionally, the authors found significant decline in physical function tests of stage 4–5 CKD patients compared to stage 2–3 CKD patients (19). In that study the superiority of one test over another was not evaluated.

The abovementioned studies have contradictory results and the tests seem inadequate unless assisted by more than one physical function assessment tool.

In 2011 the SPPB was used to measure physical performance in 375 hemodialysis patients for the first

time. The association of SPPB and eGFR was not evaluated but older age, black race, diabetes mellitus, and peripheral arterial disease were found to be associated with poorer scores on the SPPB in hemodialysis patients. Older age was already known to be associated with worse SPPB scores, so these results were not surprising. Furthermore, as this study included only patients on hemodialysis, the results cannot be generalized to all CKD patients (20). In another study performed with 486 patients  $\geq 65$  years of age in 2012, eGFR was found to be independently associated with SPPB total score (21). A more comprehensive analysis including 1111 CKD patients of all stages was performed in 2013 and worse SPPB score was found to be independently associated with the severity of renal dysfunction (12). Finally, in the CAN-FIT study published in 2015, 217 nondialysis patients with CKD of stages 4 and 5 were evaluated with the SPPB. Of the 217 patients 56% had scores of  $< 10$ , whereas 44% had scores of  $\geq 10$  and the mean score was 8.04. The SPPB was found to be worse in older patients, females, and diabetics but was not correlated with eGFR (22). Although the SPPB was demonstrated to be useful to evaluate physical function in CKD in all of the studies above and was moreover found to be independently associated with renal function in 2 of them (12,21), it has not been compared to other physical function measurement tools and none of the studies introduced the independency of the SPPB from age in CKD.

The results of our study revealed that the SPPB can be used to interpret the functional status of CKD patients independent of age. Moreover, comparison of the SPPB with other popularly used physical function assessment tools was performed and the superiority of the SPPB was demonstrated. On the other hand, the present study could not demonstrate a difference between SPPB scores of different CKD stages. The similarity of physical function test results between all CKD stages was surprising for the authors. The patients were admitted to the study in consecutive order and the physical medicine and rehabilitation specialist who performed the tests was trained, single, and blind. However, these tests were not developed specifically for CKD patients, so they may not be sensitive enough to demonstrate minimal changes between the groups. This may be an explanation. Moreover, this may also be associated with the low patient numbers in the groups, especially in stage 5.

The most important limitation of this study is the cross-sectional design, which precludes to follow the changes in SPPB results over time. Moreover, the number of stage 5 patients ( $n = 17$ ) was low and the number of all patients was also relatively low for such a prevalent disease. Apart from the design and study group limitations, there is an important handicap about the control group. Due

to the sample from which the control group was selected (healthy volunteers from the hospital staff), the mean age and the mean BMI of the control group were significantly lower. This may be estimated as an unintended bias and the results should be assessed with caution. Moreover, laboratory analysis results of the patients that may influence the functional status were not studied. Future longitudinal studies of large patient groups and matched controls are needed.

In conclusion, the SPPB, assessing lower extremity function in three dimensions (rising from a chair repetitively, stance, and walking speed), is both a more

comprehensive and more sensitive tool for evaluating functional decline in CKD patients compared with the other evaluation methods. It seems to be worse in CKD patients independent of age. Although the SPPB is a tool originally developed for geriatric physical function assessment and results get worse with age, the demonstration of the SPPB as a physical function assessment tool independent of age in CKD patients is important. As a result the SPPB is a promising, easily applicable, inexpensive, and sensitive tool that can indicate functional decline independent of age in CKD patients and it can be used in clinical practice to monitor these patients easily.

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