

ORIGINAL ARTICLE

## Correlations of sarcopenia with phase angle and Timed Up and Go test in patients on maintenance hemodialysis

Shinobu Kawasaki<sup>1,2)</sup>, Eiki Tsushima<sup>2)</sup>, Hisao Saitoh<sup>3)</sup>, and Tadashi Suzuki<sup>3)</sup>

### Abstract

**Objective:** This study aimed to investigate the correlations of sarcopenia with phase angle (PhA) and timed up and go test (TUG) in patients on maintenance hemodialysis (MHD).

**Methods:** A total of 133 patients (median age = 67.3 [59.3-72.7] years, 89 males) who underwent hemodialysis 2-3 times per week between July and September 2019 at Oyokyo Hirosaki Hospital were included. Subject demographic and clinical data were collected. Handgrip strength (HGS) and TUG were measured. Body composition was measured using bioelectrical impedance analysis to determine appendicular skeletal muscle mass (ASM) and PhA. Diagnostic criteria from the Asian Working Group for Sarcopenia 2019 (AWGS2019) were used for confirming sarcopenia. Logistic regression analysis was used to examine the factors associated with sarcopenia. Single correlation analysis and multiple regression analysis were used to examine the factors associated with PhA and TUG.

**Results:** The prevalence of sarcopenia was 37.6%. Predictors for sarcopenia were age, body mass index (BMI), and PhA. Factors associated with PhA were HGS, creatinine, the geriatric nutritional risk index (GNRI), and HD vintage, while factors associated with TUG were age, BMI, and PhA.

**Conclusion:** PhA is a predictor of both sarcopenia and TUG, and the predictors of TUG are the same as those of sarcopenia.

Hirosaki Med. J. 73 : 79–89, 2023

**Key words:** hemodialysis; sarcopenia; phase angle; TUG.

### Introduction

According to the Japanese Society for Dialysis Therapy<sup>1)</sup>, there were 347,671 patients on chronic dialysis (average age = 69.4 years) in Japan as of the end of 2020. The data showed an increased number of patients aged 70 years and over relative to the total number of patients and the average age. Of all types of dialysis treatment, hemodialysis (HD) accounted for the largest proportion at 49.3%. The most common underlying disease leading to dialysis was diabetic nephropathy at 39.5%.

Sarcopenia is a progressive systemic skeletal muscle disorder characterized by decreasing skeletal muscle mass, muscle strength, and

physical ability. The physical impairments of sarcopenia are associated with an increased risk of adverse outcomes<sup>2, 3)</sup>. Patients with chronic kidney disease (CKD) develop protein-energy wasting (PEW) due to the accumulation of uremic toxins, malnutrition, inflammation, and hypercatabolism, and as a result, they are likely to develop sarcopenia<sup>4)</sup>. To date, several diagnostic criteria for sarcopenia have been proposed. The diagnostic criteria of the Asian Working Group for Sarcopenia in 2014 (AWGS2014)<sup>5)</sup> have been used in Japan and include low appendicular skeletal muscle mass (ASM), low handgrip strength (HGS), and low physical performance. In 2019, the cut-off value of HGS for males was revised from 26 kg to 28 kg. Currently, the

<sup>1)</sup> Department of Rehabilitation Therapy, Oyokyo Kidney Research Institute, Hirosaki Hospital

<sup>2)</sup> Hirosaki University Graduate School of Health Sciences

<sup>3)</sup> Department of Urology, Oyokyo Kidney Research Institute, Hirosaki Hospital

Correspondence: S. Kawasaki

Received for publication, November 22, 2022

Accepted for publication, January 24, 2023

✉ : Shinobu Kawasaki Department of Rehabilitation Therapy, Oyokyo Kidney Research Institute, Hirosaki Hospital Hirosaki, Japan

E-mail : baby.mutuki0111@eos.ocn.ne.jp

revised standard (AWGS2019)<sup>2)</sup> is now commonly used. According to recent domestic survey reports that used the AWGS2019 diagnostic criteria, the prevalence of sarcopenia among patients on maintenance hemodialysis (MHD) is approximately 60%<sup>6)</sup> to 64.1%<sup>7)</sup>. The rate is considerably high than that in community-dwelling older adults (14.1%)<sup>8)</sup>.

The phase angle (PhA) is the arc-tangent value of the capacitive reactance of the cell membrane (cell membrane-specific resistance) divided by the resistance of the body to electric current (water and electrolytes in body fluids and tissues). The PhA can be determined using a body composition analysis device based on bioelectrical impedance analysis (BIA). PhA reflects the completeness of the cell membrane and the nutritional status of the body, and it is attracting attention as a marker for predicting the prognosis and mortality of various diseases, including CKD<sup>9-11)</sup>.

Timed up and go test (TUG) is a physical performance test for the integrated assessment of walking ability, dynamic balance, and agility in the elderly<sup>12)</sup>, and has shown high measurement reliability in MHD patients<sup>13)</sup>. However, The European Working Group on Sarcopenia in Older People 2 (EWGSOP2)<sup>3)</sup> and the AWGS2019<sup>2)</sup> have different views on whether to include TUG as a diagnostic tool for sarcopenia. Importantly, despite its inclusion in the EWGSOP2, TUG is not included in the AWGS2019.

To prevent sarcopenia in patients on MHD, it is important to clarify the status of muscle mass, muscle strength, and physical performance. Many observational studies have shown their reduction in MHD patients with sarcopenia<sup>14)</sup>, and also suggested that PhA is a predictor of sarcopenia<sup>15)</sup>. However, no studies have examined the relationship between sarcopenia, PhA and TUG, thus their mutual relationship remains unclear. By clarifying these relationships, PhA and TUG may become clinically useful

parameters and tools for identifying and/or preventing sarcopenia in patients on MHD. The present study aimed to clarify the correlations of sarcopenia with PhA and TUG in patients on MHD.

## Subjects and methods

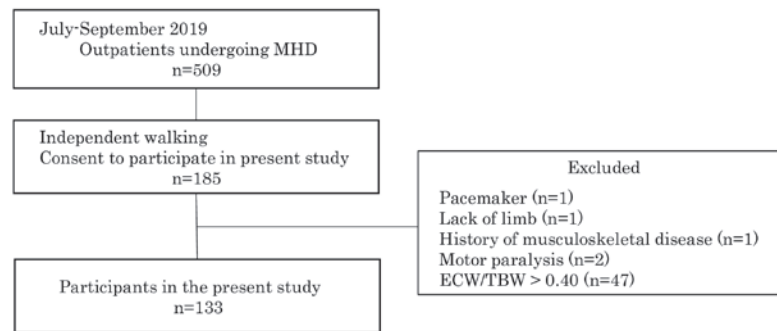
### Study design and subjects

This cross-sectional observational study was conducted at the Oyokyo Kidney Research Institute, Hirosaki Hospital (Aomori, Japan). Subjects were recruited from 509 outpatients undergoing HD 2-3 times per week between July and September 2019. Of the 509 patients, 185 self-ambulatory patients consented to participate in this study. Of these, 133 patients (89 males and 44 females) were finally included in the study. A total of 52 patients with the following conditions were excluded because they were unsuitable for measurement: installed pacemaker, lower limb amputation, musculoskeletal diseases and motor paralysis related to locomotive ability, and suspected edema (with an extracellular water/whole body water ratio of >0.4 in the most recent body composition measurement) (Figure 1).

This study was approved by the ethics committees of the Hirosaki University Graduate School of Health Sciences (Approval No.:2018-050) and the Oyokyo Kidney Research Institute. In addition, subjects were given an oral and written explanation of the study in advance, and their consent to participate in the study was obtained.

### Data collection

The demographic data, and the most recent blood biochemistry test values were collected from the patient database and medical records for 2019 for each subject. The demographic data included age, gender, dialysis start date, height, and the underlying disease leading to HD. The



**Figure 1** Study flow diagram.

MHD ; maintenance hemodialysis, ECW/TBW ; extracellular water / total body water

blood biochemistry test values before the subjects underwent HD included hemoglobin, serum albumin, serum creatinine, potassium, inorganic phosphate, and glucose. In addition, the body mass index (BMI, an index of physical constitution and obesity) and the geriatric nutritional risk index (GNRI, which reflects nutritional status) were calculated using the relevant formulas. The body weight immediately after the completion of water removal was used in the calculations.

$$\text{GNRI} = 14.89 \times \text{Albumin (g/dl)} + 41.7 \times (\text{Body weight (kg)} / \text{Ideal body weight (kg)})$$

$$\text{Male: Ideal body weight (kg)} = \text{Height (cm)} - 100 - ((\text{Height (cm)} - 150) \div 4)$$

$$\text{Female: Ideal body weight (kg)} = \text{Height (cm)} - 100 - ((\text{Height (cm)} - 150) \div 2.5)$$

The ratio of body weight/ideal body weight was set to 1 for subjects whose body weight was higher than the ideal body weight.

## Measurements

### Body composition

To determine PhA and ASM (appendicular skeletal muscle mass/height<sup>2</sup>), the subject's body composition was measured using BIA after the completion of water removal by HD using the In Body S10 (InBody Japan Inc, Tokyo, Japan). Measurements were performed with the subject in a supine position according to the manufacturer's instructions.

### Handgrip strength

The HGS was measured using a Smedley digital hand dynamometer (T.K.K.5401; Takei, Niigata, Japan) before the subjects underwent HD. After the grip length of the hand dynamometer was adjusted for each subject, the subject was instructed to hold the grip with his/her utmost strength in a standing position. Measurements were performed once for each of the left and right hand and the average value was determined.

### Timed up and go test

The subjects were instructed to stand up from sitting on a chair, upon hearing the cue, "start", and begin walking at a comfortable and safe speed, turn around at a landmark 3 m away, and then, sit back in the chair. In this test, the time required for each subject to complete the series of movements was measured with a stopwatch. The measurement was performed once before the subject underwent HD.

### Diagnosis of sarcopenia

The criteria of AWGS2019<sup>2)</sup> were used for the diagnosis of sarcopenia. According to AWGS2019, a cut-off value was set for each of the measurements, including ASM, HGS, and physical performance, and sarcopenia is diagnosed when a patient demonstrates low HGS

or low physical ability in addition to low ASM. Furthermore, severe sarcopenia is diagnosed when all of the three items fall below the cut-off values. In the present study, the diagnosis of sarcopenia was made according to the following cut-off values for HGS and ASM:

HGS: male < 28 kg, female < 18 kg

ASM: male < 7.0 kg/m<sup>2</sup>, female < 5.7 kg/m<sup>2</sup>

In this study, we did not identify those with "severe sarcopenia", as we did not conduct the necessary physical performance tests specified in the AWGS2019 (6-meter walk, 5-times chair stand, or short physical performance battery).

### Statistical analysis

The Shapiro-Wilk test was applied to ensure that the data followed a normal distribution. The subjects were divided into two groups according to gender or the presence or absence of sarcopenia. Differences between the two groups were analyzed using the two-sample t-test or Mann-Whitney U-test. The distributions of males and females in the two groups were compared using the  $\chi^2$ -test.

Factors affecting the presence or absence of sarcopenia were analyzed by multiple logistic regression analysis. The explanatory variables included age, HD vintage, BMI, PhA, GNRI, creatinine, and TUG. ASM and HGS were not included in the explanatory variables as they are diagnostic components of sarcopenia. The relationships between PhA, TUG, and other variables were determined by the correlation coefficients. In addition, multiple regression analysis was used to clarify the factors associated with PhA and TUG, respectively. Age, HD vintage, BMI, GNRI, creatinine, and HGS were used as explanatory variables for both PhA and TUG, ASM was excluded from the explanatory variables to avoid multicollinearity with HGS.

R2.8.1 (CRAN; freeware) was used for statistical analysis, and the significance level was

set at 5% for all tests.

## Results

### 1. Subject characteristics (Table 1)

Of the 133 subjects, there were 89 males, accounting for 67% of the subjects. The median age [interquartile range] was 67.3 [59.3-72.7] years. Those over the age of 70 years accounted for approximately 40% of the subjects. The average HD vintage was 5.7 [2.9-13.0] years. Among the underlying diseases leading to HD, diabetic nephropathy was the most common, accounting for 37.6% of the subjects. Gender differences were observed in ASM, PhA, creatinine, and HGS, and their values were significantly higher in males than in females ( $p < 0.001$ ).

### 2. Comparison of variables between patients with and without sarcopenia (Table 2)

The number of subjects with ASM and HGS below the AWGS2019 cut-off values were 82 (61.7%) and 63 (47.4%), respectively, and 50 (37.6%) who were both below the cutoff were diagnosed with sarcopenia. There was no significant difference in the gender distribution between the sarcopenia and non-sarcopenia groups.

The age of subjects in the sarcopenia group was  $70.2 \pm 11.3$  years (mean  $\pm$  standard deviation), which was significantly older than  $64.4 \pm 13.1$  years in the non-sarcopenia group ( $p < 0.001$ ). Also, the proportion of subjects with sarcopenia was higher in older subjects.

The sarcopenia group had significantly lower values of not only ASM and HGS, but also BMI, PhA, GNRI, albumin, and creatinine than the non-sarcopenia group.

### 3. Predictors of sarcopenia (Table 3)

Logistic regression analysis selected PhA (odds ratio (OR): 0.366 [95% CI: 0.192-0.700],

**Table 1** Demographic and Clinical Characteristics

Variables	Total (n=133)	Male (n=89)	Female (n=44)	p-Value
Age (years)	67.3 [59.3-72.7]	67.9 [59.0-74.0]	65.0 [60.0-70.7]	0.235
40-49 years (%)	6.0	7.9	2.3	
50-59 years (%)	20.3	19.1	22.7	
60-69 years (%)	36.1	31.5	45.5	
70-79 years (%)	33.1	36.0	27.3	
80-89 years (%)	4.5	5.6	2.3	
HD-vintage (years)	5.7 [2.9-13.0]	4.9 [2.8-9.8]	6.8 [3.5-15.2]	0.100
Primary disease				
diabetic nephropathy (%)	37.6	41.6	29.5	
chronic glomerulonephritis (%)	16.5	12.4	25	
nephrosclerosis (%)	15.8	19.1	9.1	
polycystic kidney disease (%)	4.5	4.5	4.5	
IgA nephropathy (%)	3.8	2.2	6.8	
nephrotic syndrome (%)	2.3	1.1	4.5	
others (%)	8.3	9	6.8	
unknown (%)	11.3	10.1	13.6	
BMI (kg/m <sup>2</sup> )	22.9 [20.8-25.1]	23.0 [21.0-25.3]	22.5 [20.1-24.3]	0.319
ASM (kg/m <sup>2</sup> )	6.4 [5.7-7.0]	6.7 [6.3-7.2]	5.4 [5.1-5.9]	<0.001
PhA (°)	5.0 ± 0.7	5.2 ± 0.7	4.7 ± 0.7	<0.001
GNRI	94.4 ± 4.5	94.9 ± 4.5	93.4 ± 4.5	0.070
Hemoglobin (g/dL)	11.6 ± 0.9	11.6 ± 0.9	11.5 ± 1.0	0.459
Albumin (g/dL)	3.7 ± 0.2	3.7 ± 0.2	3.6 ± 0.3	0.159
Creatinine (mg/dL)	11.5 [9.7-13.3]	12.1 [9.8-13.8]	10.6 [9.3-11.7]	<0.001
Potassium (mEq/L)	4.8 ± 0.7	4.8 ± 0.8	4.8 ± 0.7	0.825
Inorganic phosphate (mg/dL)	6.1 ± 1.5	6.0 ± 1.6	6.1 ± 1.5	0.873
Glucose (mg/dL)	122.0 [103.0-147.0]	125.0 [108.0-147.0]	112.0 [98.8-144.3]	0.091
HGS (kg)	26.2 ± 8.4	29.9 ± 7.4	18.6 ± 4.2	<0.001
TUG (seconds)	9.1 [8.0-10.3]	9.1 [8.0-10.3]	9.0 [8.2-9.9]	0.552

Parameter values are shown as percentage, mean ± 1 standard deviation or median [interquartile range].

HD: Hemodialysis, BMI: Body mass index, ASM: Appendicular skeletal muscle mass,

PhA: Phase angle, GNRI: Geriatric nutritional risk index, HGS: Handgrip strength, TUG: Timed up and go test

p=0.002), BMI (OR: 0.807 [95% CI: 0.691-0.942], p=0.006), and age (OR: 1.061 [95% CI: 1.011-1.114], p=0.016) as predictors for sarcopenia, while TUG was not selected.

#### 4. Correlations between PhA, TUG and other variables (Table 4)

PhA showed significant positive correlations with ASM, creatinine, and HGS in both the sarcopenia and non-sarcopenia groups. In the non-sarcopenia group, PhA also showed a significant negative correlation with HD vintage and a positive correlation with BMI.

TUG (n=133) showed a significant positive correlation with age and BMI, and a negative correlation with PhA and albumin. A significant

correlation between BMI and TUG was found in both the sarcopenia and non-sarcopenia groups. In the non-sarcopenia group, TUG showed a significant positive correlation with age and negative correlations with GNRI, albumin, and creatinine.

#### 5. Factors predicting PhA and TUG (Table 5)

Multiple regression analysis showed that HGS ( $\beta=0.425$ ,  $p<0.01$ ), creatinine ( $\beta=0.276$ ,  $p<0.01$ ), GNRI ( $\beta=0.159$ ,  $p<0.05$ ), and HD vintage ( $\beta=-0.151$ ,  $p<0.05$ ) were associated with PhA, and that BMI ( $\beta=0.077$ ,  $p<0.01$ ), PhA ( $\beta=-0.196$ ,  $p<0.05$ ), and age ( $\beta=0.196$ ,  $p<0.05$ ) with TUG.

**Table 2** Comparison of variables with and without sarcopenia

Variables	Non-Sarcopenia (n=83)	Sarcopenia (n=50)	p-Value
male/female (n)	58/25	31/19	0.349
Age (years)	64.4 ± 13.1	70.2 ± 11.3	<0.001
~59 years (n)	35	8	0.006
60-69 years (n)	32	16	
70-79 years (n)	22	22	
80-89 years (n)	2	4	
HD-vintage (years)	4.2 [2.8-11.9]	7.0 [3.3-13.3]	0.313
DM+/- (n)	36/47	18/32	0.402
BMI (kg/m <sup>2</sup> )	23.7 [21.5-26.0]	22.0 [20.1-23.9]	0.006
ASM (kg/m <sup>2</sup> )	6.9 [6.0-7.3]	6.1 [5.2-6.5]	<0.001
< cutoff values (n)	32	50	
PhA (°)	5.3 ± 0.7	4.7 ± 0.6	<0.001
~4.6° (n)	19	25	<0.001
4.7° ~5.3° (n)	26	18	
5.4° ~ (n)	38	7	
Hemoglobin (g/dL)	11.5 ± 1.0	11.7 ± 0.9	0.165
GNRI	95.3 ± 4.0	92.8 ± 4.8	0.001
Albumin (g/dL)	3.7 [3.6-3.9]	3.6 [3.5-3.7]	0.014
Creatinine (mg/dL)	11.8 ± 2.9	10.7 ± 2.0	0.012
Potassium (mEq/L)	4.8 [4.3-5.3]	4.9 [4.4-5.3]	0.516
Inorganic phosphate (mg/dL)	6.1 ± 1.5	6.0 ± 1.5	0.709
Glucose (mg/dL)	125.0 [108.5-159.0]	114.0 [98.8-130.80]	0.052
HGS (kg)	30.8 [22.7-35.2]	21.3 [16.8-25.2]	<0.001
< cutoff values (n)	13	50	
TUG (seconds)	9.0 [8.0-10.0]	9.2 [8.4-10.9]	0.138

Parameter values are shown as number, mean ± 1 standard deviation or median [interquartile range]. HD: Hemodialysis, DM: Diabetes Mellitus. BMI: Body mass index, ASM: Appendicular skeletal muscle mass, PhA: Phase angle, GNRI: Geriatric nutritional risk index, HGS: Handgrip strength, TUG: Timed up and go test

**Table 3** Logistic regression analysis for the prediction of sarcopenia (n=133)

Covariates	Coefficient (β)	Odds Ratio	95% CI	p-Value
PhA (°)	- 1.004	0.366	0.192 - 0.700	0.002
BMI (kg/m <sup>2</sup> )	- 0.214	0.807	0.691 - 0.942	0.006
Age (years)	0.065	1.061	1.011 - 1.114	0.016
TUG (sec)	0.194	1.214	0.981 - 1.501	0.073

The dependent variable was sarcopenia. The Independent variables were Age, HD-vintage, BMI, PhA, GNRI, Creatinine, TUG. 95% CI: 95% confidence interval

## Discussion

Figure 2 shows an overview of the relationships among the items.

### 1. Characteristics of subjects with sarcopenia and predictive factors of sarcopenia

The prevalence of sarcopenia in the present study was 37.6%, which was higher than 14.1% in community-dwelling elderly<sup>8)</sup>, but lower than 60% and 64.1% of MHD patients reported by

Matsuzawa et al.<sup>6)</sup> and Kurajoh et al.<sup>7)</sup>, respectively. The subjects in our study were on average 10 years younger than in previous reports, and the lower proportion of HGS below the cutoff contributed to difference in the prevalence.

The sarcopenia group, compared to the non-sarcopenia group, was older and demonstrated significantly lower BMI, GNRI, albumin, creatinine, and PhA. However, there was no

**Table 4** Correlation coefficients between phase angle ,TUG and other variables

Variables	Phase Angle			TUG		
	Total (n=133)	Non-Sarcopenia (n=83)	Sarcopenia (n=50)	Total (n=133)	Non-Sarcopenia (n=83)	Sarcopenia (n=50)
Age (years)	- 0.287**	- 0.207	- 0.054	0.240**	0.223*	0.190
HD-vintage (years)	- 0.225**	- 0.216*	- 0.175	- 0.118	- 0.142	- 0.117
BMI (kg/m <sup>2</sup> )	0.282**	0.245*	0.107	0.230**	0.224*	0.383**
ASM (kg/m <sup>2</sup> )	0.510**	0.392**	0.461**	0.035	0.086	0.173
PhA (°)	-	-	-	- 0.207*	- 0.216	- 0.053
GNRI	0.318**	0.268*	0.250	- 0.089	- 0.220*	0.196
Hemoglobin (g/dL)	0.129	0.164	0.268	- 0.036	- 0.009	- 0.153
Albumin (g/dL)	0.173*	0.062	0.214	- 0.211*	- 0.337**	0.057
Creatinine (mg/dL)	0.436**	0.397**	0.404**	- 0.165	- 0.220*	0.134
Potassium (mEq/L)	0.086	0.167	0.045	- 0.030	- 0.180	0.184
Inorganic phosphate (mg/dL)	0.066	0.052	0.072	- 0.022	- 0.115	0.124
Glucose (mg/dL)	0.180*	0.201	- 0.147	- 0.105	- 0.081	- 0.122
HGS (kg)	0.575**	0.514**	0.492**	- 0.157	- 0.213	0.043
TUG (seconds)	- 0.207*	- 0.216	- 0.053	-	-	-

\*: p<0.05 \*\*: p<0.01 BMI: Body mass index, ASM: Appendicular skeletal muscle mass, PhA: Phase angle, GNRI: Geriatric nutritional-index, HGS: Handgrip strength, TUG: Timed up and go test

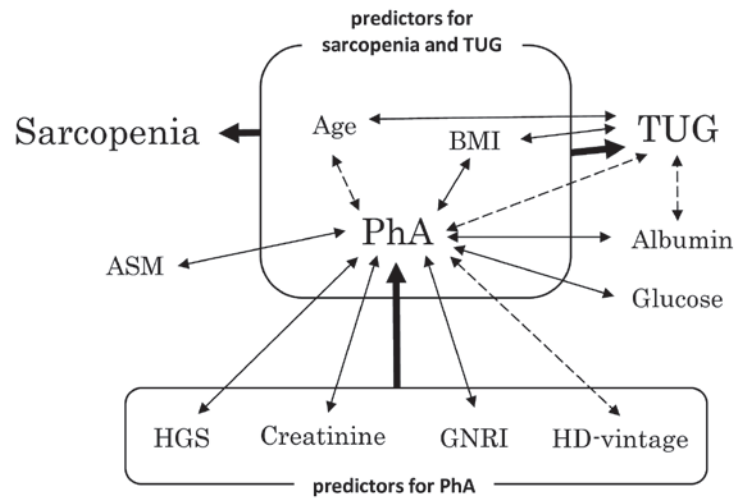
**Table 5** Summary of multiple regression analysis for PhA and TUG

<PhA>		
Independent variables	Standardized partial regressin coefficient ( $\beta$ )	p-Value
HGS (kg)	0.425	<0.001
Creatinine (mg/dL)	0.276	<0.001
GNRI	0.159	0.023
HD-vintage (years)	- 0.151	0.046
<TUG>		
Independent variables	Standardized partial regressin coefficient ( $\beta$ )	p-Value
BMI	0.077	0.001
PhA	- 0.196	0.028
Age	0.196	0.023

< >: The dependent variable. The independent variables were Age, HD vintage, BMI, GNRI, Creatinine, HGS, PhA or TUG.

difference in the TUG time between the two groups. Sarcopenia has been described to be associated with aging<sup>5)</sup>, and the items with low values in the sarcopenia group have been shown to decrease in patients with sarcopenia and malnutrition<sup>10, 16)</sup>. Logistic regression analyses showed that age (OR: 1.061 [95% CI: 1.011-1.114], p=0.016), BMI (OR: 0.807 [95% CI: 0.691-0.942], p=0.006), and PhA (OR: 0.366 [95% CI: 0.192-0.700], p=0.002) were predictive factors of sarcopenia, which were concurred with a previous report<sup>15)</sup>. Furthermore, we confirmed

that a decreased PhA in subjects with sarcopenia, and a high sarcopenia prevalence in subjects with low PhA<sup>10)</sup>. These results indicated a negative correlation between sarcopenia and PhA, and PhA likely a predictive marker of sarcopenia. In contrast, a previous study indicated that PhA was an inadequate predictor of sarcopenia. Santana et al.<sup>17)</sup> investigated the association between sarcopenia and PhA in 148 hospitalized patients with coronary artery disease (71.6  $\pm$  7.6 years) and reported that PhA had a low predictive ability to explain muscle mass, muscle



**Figure 2** Factors associated with sarcopenia, PhA and TUG

predictors for sarcopenia and TUG: Age, BMI, PhA

predictors for PhA: HGS, Creatinine, GNRI, HD-vintage

➔: the direction of impact, ↔: positive correlation, ↔: negative correlation

TUG: Timed up and go test, BMI: Body mass index, PhA: Phase angle, HGS: Handgrip strength, GNRI: Geriatric nutritional risk index, HD: Hemodialysis, ASM: Appendicular skeletal muscle mass,

strength, and functional capacity. In their study, 70% of sarcopenia patients had severe sarcopenia, and thus, the subject bias may have weakened the predictive power of PhA.

The TUG has been described as a highly accurate tool for predicting sarcopenia in older hospitalized patients<sup>18)</sup> and as a useful screening tool for frailty in older MHD patients<sup>19)</sup>.

However, the present study showed no difference in TUG between the sarcopenia and non-sarcopenia groups, and TUG was not selected as a factor predicting sarcopenia. Podsiadlo *et al.*<sup>12)</sup> reported that older people with TUG times less than 20 seconds have no problems with basic daily locomotion, and TUG times may have curvilinear relationships with walking speed, balance test scores, and ADL. In the present study, 72% of subjects had a TUG time less than 10 seconds, and only one exceeded 20 seconds (21.7 seconds). Therefore, the small variability in TUG times and the method of statistical analysis assuming linear regression

may have affected the prediction of the relationship between TUG and sarcopenia.

## 2. Factors associated with PhA and TUG

### (1) PhA

Multiple regression analysis showed that HGS, creatinine and GNRI were positively associated with PhA, and HD vintage was negatively associated. PhA is known to positively correlated with body cell mass and lean body mass<sup>9-11)</sup>. Muscle strength is proportional to muscle cross-sectional area, and malnourished MHD patients have less muscle cross-sectional area and muscle weakness than those of well nourished. Most of the creatinine production is derived from muscle metabolism<sup>20)</sup>, and dialysis patients have lost the ability to excrete creatin from kidneys, therefore, serum creatinine concentrations may reflect muscle mass<sup>21)</sup>. In addition, dialysis patients are prone to malnutrition due to various factors associated with renal failure, leading to decreased GNRI<sup>4)</sup>.



Of the predictors for PhA, only HD vintage was negatively correlated with PhA. HD vintage was reported to be closely associated with the development of sarcopenia<sup>22)</sup>, and it may be the longer the HD vintage, the lower the PhA due to sarcopenia and malnutrition.

## (2) TUG

In multiple regression analysis, age, BMI and PhA were selected as factors to explain TUG time. Interestingly, all of these were predictors of sarcopenia, suggesting that TUG time were affected by the same factors with sarcopenia.

A previous study<sup>23)</sup> has also shown that TUG time lengthens with age, and it is possible that the development of sarcopenia and age-related decline in balance ability and leg muscle weakness in subjects contribute to a positive correlation. Previous studies have shown that BMI is positively correlated with ASM in the elderly<sup>24)</sup>, and that women with central obesity and high BMI have longer TUG times<sup>25)</sup>. The abdominal circumference of subjects was not measured in this study, 70% of subjects had a standard body weight with a BMI of between 18.5 and 25 kg/m<sup>2</sup>. Because low body weight and extreme obesity are thought to have adverse health effects, the large number of subjects with standard body weight likely has resulted in a positive correlation between BMI and TUG time.

In the present study, TUG showed a negative correlation with PhA, and this finding is consistent with a previous report<sup>26)</sup>. In addition, TUG has also been shown to be a predictor of number of falls on MHD patients<sup>27)</sup>. PhA is positively correlated with muscle strength, and muscle weakness is one of the causes of prolonged TUG time and falls. These reflect a negative relationship between PhA and TUG time.

Serum albumin levels are a valid measure of nutritional status in PEW. In this study, the sarcopenia group had significantly lower albumin

levels than the non-sarcopenia group, and there was a negative correlation between albumin and TUG time. Undernourished MHD patients have been shown to have lower muscle strength than well-nourished patients<sup>28)</sup>, and undernutrition-induced muscle weakness may be associated with longer TUG time.

## Limitations

This was a cross-sectional study conducted at one facility, with a small number of subjects. Although the subjects were limited to ambulatory patients, their walking speed, walking distance, and use of assistive devices were not considered. Also, the exercise habits and exercise activities of the subjects were unknown. As these may have affected the results of this study, caution is needed when interpreting the results. Since many confounding factors may be associated with the measurement items, in the future, further studies with larger sample sizes are necessary. Moreover, investigations of the associations between walking ability, the level of physical activities, blood and biochemistry test values, and water balance by BIA are warranted.

## Conclusion

Our finding indicates that age, BMI, and PhA are predictors of sarcopenia in patients on MHD, and that the prevalence of sarcopenia is higher with lower PhA. Also, the predictors of TUG are the same as those of sarcopenia, and PhA is negatively correlated with TUG. Sarcopenia, PhA and TUG in MHD patients are likely to be strongly related to each other, and further investigation is needed.

## Conflicts of interest

The authors have no conflicts of interest directly relevant to the content of this article.

## Acknowledgments

We would like to express our deepest gratitude to Honorary Professor Akira Ishikawa of Hirosaki University, for his invaluable guidance throughout the study. We would also like to thank the patients and staff of the Oyokyo Kidney Research Institute, Hirosaki Hospital for their cooperation in this research.

## References

- 1) Japanese Society of Dialysis Therapy. An overview of regular dialysis treatment in Japan as of Dec 31, 2020. <http://docs.jsdt.or.jp/overview/index.html>. (Accessed 23 June 2022)
- 2) Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, Jang HC, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc.* 2020;21:300-7.
- 3) Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing.* 2019;48:16-31.
- 4) Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, Franch H, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int.* 2008;73:391-8.
- 5) Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, Chou MY, et al. Sarcopenia in Asia: Consensus report of the Asian Working Group for Sarcopenia. *J Am Med Dir Assoc.* 2014; 15:95-101.
- 6) Matsuzawa R, Yamamoto S, Suzuki Y, Imamura K, Harada M, Matsunaga A, Tamaki A, et al. The clinical applicability of ultrasound technique for diagnosis of sarcopenia in hemodialysis patients. *Clin Nutr.* 2021;40:1161-7.
- 7) Kurajoh M, Mori K, Miyabe M, Matsufuji S, Ichii M, Morioka T, Kizu A, et al. Nutritional Status Association With Sarcopenia in Patients Undergoing Maintenance Hemodialysis Assessed by Nutritional Risk Index. *Front Nutr.* 2022; 9:896427.
- 8) Kitamura A, Seino S, Abe T, Nofuji Y, Yokoyama Y, Amano H, Nishi M, et al. Sarcopenia: prevalence, associated factors, and the risk of mortality and disability in Japanese older adults. *J Cachexia Sarcopenia Muscle.* 2021;12:30-8.
- 9) Marra M, Sammarco R, De Lorenzo A, Iellamo F, Siervo M, Pietrobelli A, Donini LM, et al. Assessment of Body Composition in Health and Disease Using Bioelectrical Impedance Analysis (BIA) and Dual Energy X-Ray Absorptiometry (DXA): A Critical Overview. *Contrast Media Mol Imaging.* 2019;2019:3548284.
- 10) Di Vincenzo O, Marra M, Di Gregorio A, Pasanisi F, Scalfi L. Bioelectrical impedance analysis (BIA)-derived phase angle in sarcopenia: A systematic review. *Clin Nutr.* 2021;40:3052-61.
- 11) Garlini LM, Alves FD, Ceretta LB, Perry IS, Souza GC, Clausell NO. Phase angle and mortality: a systematic review. *Eur J Clin Nutr.* 2019;73:495-508.
- 12) Podsiadlo D, Richardson S. The timed 'Up & Go': a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc.* 1991;39:142-8.
- 13) Ortega-Perez de Villar L, Martinez-Olmos FJ, Junque Jimenez A, Amer-Cuenca JJ, Martinez-Gramage J, Mercer T, Segura-Orti E. Test-retest reliability and minimal detectable change scores for the short physical performance battery, one-legged standing test and timed up and go test in patients undergoing hemodialysis. *PLoS One.* 2018;13:e0201035.
- 14) Sabatino A, Cuppari L, Stenvinkel P, Lindholm B, Avesani CM. Sarcopenia in chronic kidney disease: what have we learned so far? *J Nephrol.* 2021;34:1347-72.
- 15) Ding Y, Chang L, Zhang H, Wang S. Predictive value of phase angle in sarcopenia in patients on maintenance hemodialysis. *Nutrition.* 2022;94: 111527.
- 16) Inaba M, Okuno S, Ohno Y. Importance of Considering Malnutrition and Sarcopenia in Order

- to Improve the QOL of Elderly Hemodialysis Patients in Japan in the Era of 100-Year Life. *Nutrients*. 2021;13:2377.
- 17) Santana NM, Pinho CPS, da Silva CP, Dos Santos NF, Mendes RML. Phase Angle as a Sarcopenia Marker in Hospitalized Elderly Patients. *Nutr Clin Pract*. 2018;33:232-7.
- 18) Martinez BP, Gomes IB, Oliveira CS, Ramos IR, Rocha MD, Forgiarini Júnior LA, Camelier AA, et al. Accuracy of the Timed Up and Go test for predicting sarcopenia in elderly hospitalized patients. *Clinics*. 2015;70:369-72.
- 19) Zanotto T, Mercer TH, van der Linden ML, Koufaki P. Screening tools to expedite assessment of frailty in people receiving haemodialysis: a diagnostic accuracy study. *BMC Geriatr*. 2021; 21:411.
- 20) Keshaviah PR, Nolph KD, Moore HL, Prowant B, Emerson PF, Meyer M, Twardowski ZJ, et al. Lean body mass estimation by creatinine kinetics. *J Am Soc Nephrol*. 1994;4:1475-85.
- 21) Kanazawa Y, Nakao T, Shirota N, Nishimura M, Okada T, Ozawa M, Takagi Y. Screening of hemodialysis patients for sarcopenia based on the Ishii score. *The Japanese Society for Dialysis Therapy*. 2021;54:283-9. (In Japanese)
- 22) Ren H, Gong D, Jia F, Xu B, Liu Z. Sarcopenia in patients undergoing maintenance hemodialysis: incidence rate, risk factors and its effect on survival risk. *Ren Fail*. 2016;38:364-71.
- 23) Steffen TM, Hacker TA, Mollinger L. Age- and Gender-Related Test Performance in Community-Dwelling Elderly People: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and Gait Speeds. *Phys Ther*. 2002;82:128-37.
- 24) Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. *J Gerontol A Biol Sci Med Sci*. 2002;57: M772-7.
- 25) Oliveira R, Leao C, Silva AF, Clemente FM, Santamarinha CT, Nobari H, Brito JP. Comparisons between Bioelectrical Impedance Variables, Functional Tests and Blood Markers Based on BMI in Older Women and Their Association with Phase Angle. *Int J Environ Res Public Health*. 2022;19:6851.
- 26) Yamada Y, Itoi A, Yoshida T, Nakagata T, Yokoyama K, Fujita H, Kimura M, et al. Association of bioelectrical phase angle with aerobic capacity, complex gait ability and total fitness score in older adults. *Exp Gerontol*. 2021;150:111350.
- 27) Shirai N, Yamamoto S, Osawa Y, Tsubaki A, Morishita S, Narita I. Dysfunction in dynamic, but not static balance is associated with risk of accidental falls in hemodialysis patients: a prospective cohort study. *BMC Nephrol*. 2022;23: 237.
- 28) Fahal IH, Bell GM, Bone JM, Edwards RH. Physiological abnormalities of skeletal muscle in dialysis patients. *Nephrol Dial Transplant*. 1997; 12:119-27.